THE BASIC CALCIUM PHOSPHATES AND RELATED SYSTEMS. SOME THEORETICAL AND PRACTICAL ASPECTS

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Contributions to our knowledge of tricalcium phosphate, tetracalcium phosphate, and the apatites (for convenience, all three of these are here included in the term "basic calcium phosphates") have come principally from those concerned with the nature and deposition of the inorganic constituents of bone or in the utilization of phosphatic materials for plant food. However, the many exceedingly ingenious and difficult investigations of the basic phosphates to be found in the literature should be of interest to all who employ physicochemical methods and techniques, especially in connection with solid-phase phenomena. Some of the most significant contributions have been made by mineralogists as a result of the occurrence in nature of many varieties of calcium phosphate. Moreover, the field of water purification and boiler feed water treatment is sadly in need of a fundamental understanding of the chemistry of these compounds, in view of the rising importance of processes involving the use or precipitation of calcium phosphate.

The considerable number of publications on the basic calcium phosphates attests first to the difficulties which are encountered and second to a failure to arrive at any substantial agreement on fundamentals. Since the application of the phase rule and x-rays to the study of these compounds, a great deal of useful and reliable data has been published. The purpose of this paper is to organize the available information and to present a conception of the nature of these compounds which offers a consistent explanation of their properties. It is hoped that the research necessary for clearing up some of the remaining questions in this field will be stimulated.

PART I. CALCIUM PHOSPHATE SYSTEMS[1]

Studies of calcium phosphates encounter great practical difficulties. The principal sources of trouble in thermal investigations have been discussed by Trömel (218). They are (*a*) the reactivity of the compounds, (*b*) their sensitivity to reduction, and (*c*) the high temperatures required. These conditions eliminate utensils of ceramic materials, carbon, carbides, and most metals. Trömel reports that platinum has been successfully used by others up to 1600°C. and that he himself has found rhodium to be best suited for this work. Others have been able to use iron, nickel, or zirconium oxide crucibles, depending upon the temperature (24).

Investigations of aqueous systems, on the other hand, must contend with quite a different set of problems. The time required to establish equilibrium is often considerable (12, 36, 38, 39, 59, 82, 111, 117, 132, 191, 220, 224). Bassett, for example, reports that in some cases complete equilibrium is not attained at 25°C. in 19 months (12). The size of particles usually found in the solid phase is so minute as to create difficulties in settling and filtering precipitates, in obtaining clear x-ray powder photographs, and in the use of petrographic methods (11, 12, 25, 37, 54, 66, 74, 126, 220). The extremely low solubilities of the basic phosphates (11, 12, 39, 54, 72, 82, 83, 126, 153, 196, 197) make it difficult to obtain reliable analytical results for saturated solutions. The marked effect of the solutions on glass (11, 12) presents another problem. The magnitude of this effect is illustrated by an experiment performed by one of us in which the accumulation of silica in the solid phase after a week of refluxing in a Pyrex flask was 18 per cent of the mass of the solid. In addition to the foregoing, one would suspect that the absorption of carbon dioxide by alkaline solutions, especially in the presence of excess calcium ions, would have to be guarded against. However, no mention is made of this factor.

Similar troubles have been observed for the basic calcium arsenates (44, 163, 164, 210) and for the phosphates of other metals (115, 116, 185).

I. THE BINARY SYSTEM $CaO–P_2O_5$

Much of the work done on this binary system has been beclouded by the failure to recognize the presence of a ternary system through the inclusion of small quantities of water (75). The difficulty with which

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[1] The following tabulation of terminology and numerical values is appended for the convenience of the reader.

NAME	FORMULA	MOLE RATIO $CaO:P_2O_5$	WEIGHT RATIO $P_2O_5:CaO$	REMARKS
Dicalcium phosphate....	$CaHPO_4$	2:1	1.27 :1	
Pentacalcium phosphate.		5:2	1.01 :1	Existence doubtful
α-Tricalcium phosphate*...............	$Ca_3(PO_4)_2$	3:1	0.844:1	High-temperature form (called gamma variety in first paper by Bredig *et al.*)
β-Tricalcium phosphate*...............	$Ca_3(PO_4)_2$	3:1	0.844:1	Low-temperature form; transition temperature 1180°C.
Hydroxyapatite or hydroxylapatite.........	$Ca_{10}(OH)_2(PO_4)_6$ or $3Ca_3(PO_4)_2 \cdot Ca(OH)_2$	10:3	0.760:1	Existence as a unique stoichiometric compound doubtful
Apatite................	$3Ca_3(PO_4)_2 \cdot CaX_2$	10:3	0.760:1	X = CO_3, SO_4, F, Cl, OH, etc.
Tetracalcium phosphate*...............	$Ca_4P_2O_9$	4:1	0.633:1	

* The stable existence of either form of tricalcium phosphate or of tetracalcium phosphate in the presence of water is doubtful.

last traces of water are removed from the basic phosphates is illustrated by the work of Schleede, Schmidt, and Kindt (191), who ignited hydroxyapatite preparations and found that, in the absence of excess lime, the elimination of water was not complete under 1500°C. Trömel (218) has also shown that hydroxyapatite can be formed from binary mixtures by reaction with water vapor at temperatures as high as 1050°C! This stability of hydroxyapatite to high temperatures explains why Bassett and others always found their analyses falling short of 100 per cent even after the usual ignitions at about 900°C. This behavior was early discovered, but the profound phase changes caused by traces of moisture have been only recently recognized.

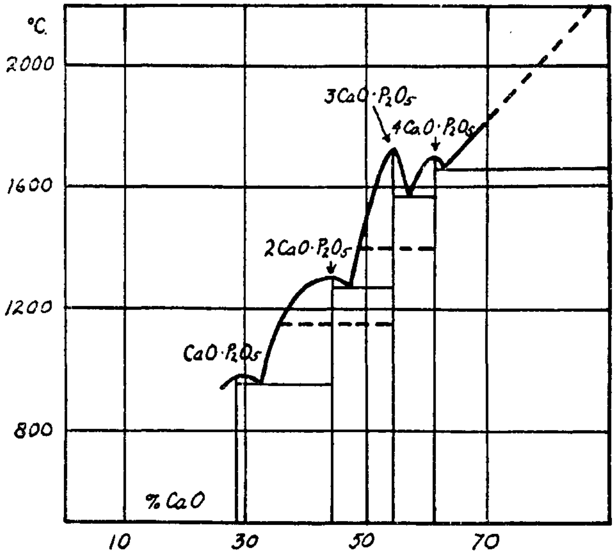

Fig. 1

The binary diagram worked out by Trömel is reproduced in figure 1. The temperature measurements were not precise enough (±20° at 1700°C.) to enable Trömel to be certain whether or not metaphosphate or pyrophosphate had congruent melting points, but that tri- and tetracalcium phosphates melted congruently was clearly indicated. The presence in the binary system of a molecular species with the formula $Ca_3(PO_4)_2$ has been thoroughly established by Trömel and his coworkers (119, 120, 217, 218, 219, 220) and by Bredig, Franck, and Füldner (24, 25). Schneiderhöhn (218) reports that $Ca_3(PO_4)_2$ exists in two enantiotropic forms with a transition point between 1250° and 1500°C. This is confirmed in a paper published almost simultaneously by Bredig *et al.* (24), who locate the reversible transformation temperature at about 1180°C.[2]

Bredig *et al.* (25) have also shown that the alpha-beta transformation of tricalcium phosphate is greatly affected by the presence of moisture and excess calcium oxide. When the alpha-form, containing excess calcium oxide, was ignited in the absence of moisture, the beta lattice did not appear until the temperature had been lowered below 840°C., but in the presence of ordinary atmospheric water vapor, the conversion of alpha to beta occurred at the usual temperature of about 1200°C. The amount of water vapor required was remarkably small,—about 0.1 to 0.2 per cent. α-Tricalcium phosphate showed no reluctance to transformation until excess calcium oxide was present. The authors concluded, therefore, that the alpha lattice was stabilized by calcium oxide which,

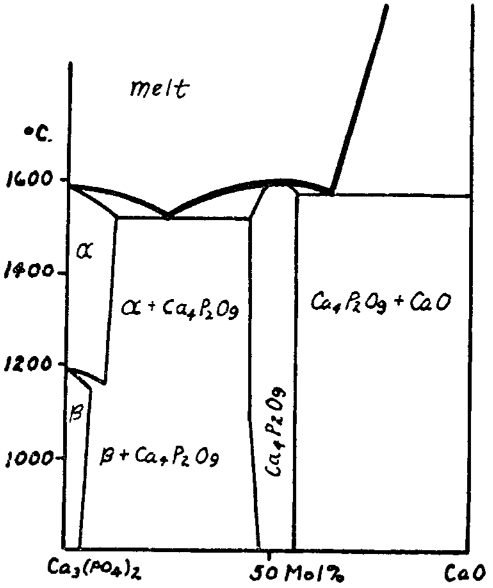

FIG. 2

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[2] In the binary system of Bredig *et al.* (24) the term "alpha phase" is applied to all compositions showing an apatite lattice, and the tricalcium phosphate stable at the higher temperature is called the gamma variety. In a later publication Bredig and his associates (25) agree with Trömel that the apatites have no place in the binary system and change their notation to conform with his. The variety of tricalcium phosphate which is stable at higher temperatures is called "alpha-tricalcium phosphate" by Trömel and his terminology will be followed in this paper.

however, could be eliminated by reaction with water and tricalcium phosphate to form hydroxyapatite.

The final diagram of Bredig *et al.* (25) is reproduced in figure 2 and shows almost perfect agreement with Trömel's diagram, except that some partial solubility in the solid phases is suggested. While the first diagram they proposed does not represent true equilibrium conditions, it does indicate the transformations which may be expected when ignitions are carried out in the presence of moisture and hence is reproduced in figure 3. The following equations represent typical reactions:

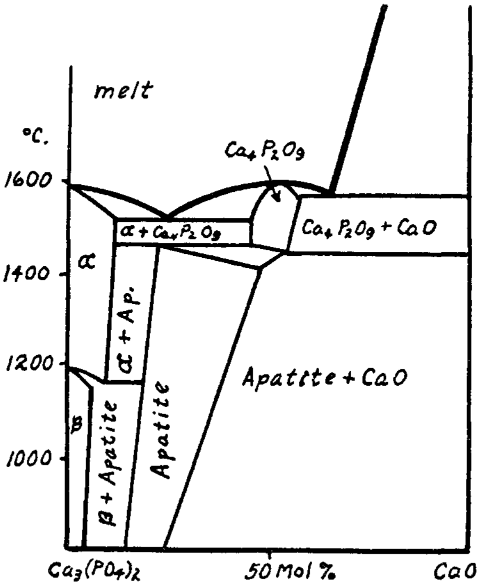

FIG. 3

$$3Ca_4P_2O_9 + H_2O \rightarrow Ca_{10}(OH)_2(PO_4)_6 + 2CaO\text{[3]}$$

$$Ca_{10}(OH)_2(PO_4)_6 \rightarrow 2Ca_3(PO_4)_2 + Ca_4P_2O_9 + H_2O\text{[4]}$$

$$3Ca_3(PO_4)_2 + CaO + H_2O \rightarrow Ca_{10}(OH)_2(PO_4)_6$$

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[3] It is interesting to note that many years ago Foerster (57) discovered that 3 moles of $Ca_4P_2O_9$ gave on ignition 2 moles of CaO, which could be extracted with sugar solutions.

[4] Schleede *et al.* (191) have shown by means of x-ray powder photographs that when hydroxyapatite is heated to a temperature sufficient to remove the last traces of moisture a mixture of $Ca_3(PO_4)_2$ and $Ca_4P_2O_9$ is obtained.

The existence of oxyapatite, $Ca_{10}O(PO_4)_6$, has often been assumed (75). Since this compound has the composition $10CaO \cdot 3P_2O_5$, it should be found between $Ca_3(PO_4)_2$ and $Ca_4P_2O_9$, but all that can be discovered in this region is a well-defined eutectic of these compounds. Although this eliminates the possibility that oxyapatite can be crystallized from a melt, there still remains the possibility that it can be formed by reaction in the solid state. Trömel (218) explored this possibility by igniting mixtures corresponding to the composition of oxyapatite at various temperatures. However, no apatites could be found when water vapor was rigorously excluded from the ignitions. In addition to this phase rule demonstration of the non-existence of oxyapatite, McConnell (144) has shown that crystallographic considerations lead to the same conclusion.

It may be said in conclusion that the foregoing description of the binary system has a high degree of reliability. The data on which the conclusions are based were gathered through the correlated use of microscopic examination, chemical analysis, x-ray methods, and heating and cooling curves.[5] These four methods of approach gave mutually consistent results.[6]

II. THE BASIC REGION OF THE SYSTEM $CaO-P_2O_5-H_2O$

How can the nature of a precipitated material be determined? Where there is some assurance that the precipitate is a single solid phase or a mixture of two phases of known composition, a chemical analysis is sufficient. Unfortunately, in a great deal of work on the basic calcium phosphates, chemical analyses were relied on to determine the nature of precipitates without realizing that more than one solid phase could be present or without knowing what these solid phases were.

Where amorphous precipitates occur, as in the system under consideration, the difficulty of determining how many solid phases are present or of identifying the solid phases is obvious. The inadequacy of chemical analyses alone and the usefulness of the phase rule, especially in connection with the identification of amorphous basic salts, was early emphasized by Miller and Kenrick (149). They pointed out that if, in a ternary system, the compositions of precipitates are plotted against the compositions of the solutions in equilibrium with the precipitates, a horizontal line would

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[5] Trömel reports (218) that calcium-rich mixtures (more than 50 per cent calcium oxide) gave no glasses even on chilling. The alpha- and beta-forms of $Ca_2P_2O_7$ and $Ca_3(PO_4)_2$ underwent transformation so slowly that heating and cooling curves were of no use in determining the transition temperatures. Since these points were only estimated by Trömel, the value determined for $Ca_3(PO_4)_2$ by Bredig, Franck, and Füldner (24) through x-ray examination of samples annealed at various temperatures is likely to be more accurate.

[6] Franck (60) and Trömel (221) have published reviews of much of the work described above.

indicate a monovariant system with a single, definite compound as the solid phase, a diagonal line would indicate a monovariant system with a solid solution of variable composition as the solid phase, and a vertical line would indicate an invariant system with two solid phases in varying proportions. This suggestion has become a standard procedure and there are innumerable examples of its application. However, there is no record of the use of this method for the basic calcium phosphates.

A large number of compounds more basic than dicalcium phosphate have been proposed solely on the basis of chemical analyses. The following is a partial list of such compounds: $Ca_4P_2O_9$ (11), $Ca_3(PO_4)_2$ (11, 12), $2CaHPO_4 \cdot Ca_3P_2O_8$ (163, 171), $5CaO \cdot 2P_2O_5 \cdot 10H_2O$ (55, 100, 186), and others (31, 171, 172). Some of these have been shown not to exist (74), and the others merit little consideration except insofar as supporting evidence is brought forward.

However, even when the phase rule is applied, certain elementary considerations must be taken into account. It is probably unnecessary to point out that the phase rule applies only to equilibrium conditions. But what does need emphasis is the danger of using time invariance of composition as a criterion for the attainment of equilibrium, especially where reaction rates are known to be very slow as they are for the basic calcium phosphates.

Another point which is sometimes neglected is the necessity for having homogeneous phases separated by sharp boundaries if the formula $P + F = C + 2$ is to be applicable. In dealing with amorphous solids, this condition is sometimes difficult to obtain, owing to surface effects such as adsorption.

The only certain criterion for equilibrium is to obtain identical results by approaching equilibrium from opposite sides. Moreover, if identical results are so obtained, it is virtually certain that adsorption effects are negligible. For if adsorption had taken place to any considerable extent, it is highly unlikely that its effect would be the same in both cases, considering the different environments on opposite sides of the equilibrium and the possibilities for particle size variation.

On the other hand, when adsorption does occur, the only certain method for detecting it and following changes in the solid phase is by means of x-rays, provided that changes in lattice dimensions are large enough to be detected.

There has been no fundamental investigation of the basic calcium phosphates which has given proper consideration to all of the foregoing factors. This undoubtedly accounts for the fact that the comparatively large amount of work done in this field is repetitious, disorganized, and contradictory.

Nevertheless, it is possible to bring some order into a seemingly bewildering situation and to resolve many of the present contradictions, if a few simple assumptions are made. *First, between dicalcium phosphate and lime, there exists, in the ternary system, a continuous series of solid solutions having an apatite lattice. It follows from this that tricalcium phosphate and hydroxyapatite do not exist in aqueous systems as unique, stoichiometric compounds.*[7] *Finally, in the words of McConnell (145), "The structure of apatite seems to be remarkably stable, permitting a number of unusual types of substitution and involving a considerable number of ions."*

These conclusions result from the critical review of the literature presented in the following sections.

A. The phase diagram

In 1908, Bassett (11) published a thorough phase rule study of the entire system at various temperatures. While his data for the isotherm at 25°C. were in good agreement with the results of previous workers (38, 39), his conclusions on the basic region were quite different. Whereas Cameron and his associates had given up the idea that tricalcium phosphate could be produced in an aqueous system in stable or metastable[8] form and had decided instead that dicalcium phosphate and lime formed a continuous series of solid solutions,[9] Bassett believed that the data showed the existence of tri- and tetra-calcium phosphates. He based his conclusion

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[7] The terms "tricalcium phosphate" and "hydroxyapatite" are very widely and very loosely used. For example, some authors use the former for any precipitate more basic than dicalcium phosphate, although such precipitates have been frequently shown to have an apatite lattice or to be mixtures of dicalcium phosphate and an apatite. Others confine the use of the term to those precipitates with P_2O_5:CaO ratios approaching that of $Ca_3(PO_4)_2$. "Hydroxyapatite" is often used with the implication that the composition $Ca_{10}(OH)_2(PO_4)_6$, or several variations, has a unique existence as a definite compound. It would be tedious and repetitious to discuss in every case what term should have been used, and on the other hand confusing to make corrections without such discussion. Consequently, original terminology is used wherever the context is sufficiently clear to avoid confusion. The term "hydroxyapatite" will be used by us to mean any apatite belonging to the system $CaO-P_2O_5-H_2O$.

[8] Cameron (38) had originally suggested the possibility of the initial precipitation of metastable tricalcium phosphate with a slow rate of change to the stable form, but gave up the idea (39) when he could find no supporting evidence. Fouretier (59) also believed that the initial precipitate was metastable tricalcium phosphate which, however, reacted to form stable hydroxyapatite. The evidence for this belief is questionable.

[9] It is interesting to note that twenty-four years later Cameron (44) made a similar assertion for the basic region of the system $CaO-As_2O_5-H_2O$.

solely on the fact that analyses for some of his solid compositions were nearly correct for these compounds.

Since the data on which his conclusions for the basic region were based were rather meager, Bassett undertook a more extended investigation (12). Realizing the danger of relying on chemical analyses alone, Bassett plotted the concentrations of CaO against the concentrations of P_2O_5 in saturated solutions and looked for discontinuities in the curve to identify the solid phases. However, no discontinuities were found for tri- and tetra-calcium phosphates. While Bassett changed his mind about $Ca_4P_2O_9$[10], he reiterated his belief in the probable existence of tricalcium phosphate over a limited range of concentrations because so many of his preparations had compositions approaching the composition of $Ca_3(PO_4)_2$. He concluded from the failure to obtain a break in his curve at the boundary between di- and tri-calcium phosphates that there was no great difference in solubility between metastable dicalcium phosphate and stable tricalcium phosphate. He believed, moreover, that these small differences in solubility also accounted for the slowness of conversion of the former into the latter.

Bassett's data have been recalculated so that they could be plotted according to variations of the suggestion of Miller and Kenrick. In figures 4 and 5, the curves *ABC*, *AGH*, and *MEF* are consistent with Bassett's stated conclusions, but the curves *CD* and *HM*, which fit the data in a fairly satisfactory fashion, show that in the regions covered by them the solid phase is a solution of variable composition, having, as has been demonstrated by others, an apatite lattice (110, 220). Although some of the points are badly spotted, there seems to be no justification for a horizontal line at $P_2O_5:CaO = 0.845$, which should appear if tricalcium phosphate has a stable existence. From *D* and *M* to *E* the solid phase is undoubtedly hydroxyapatite. The solid phase along *EF* is reported by Bassett to be heterogeneous under the microscope and is evidently a mixture of varying quantities of hydroxyapatite and calcium hydroxide.

The stable existence of tricalcium phosphate in aqueous systems is highly improbable. Many others have come to a similar conclusion (36, 37, 38, 39, 54, 110, 112, 186, 187, 223).

The experimental results obtained by Jolibois (100) at 15–18°C. with a rapid mixing method (99) have been recalculated so that they could also be plotted in figures 4 and 5. The curve so obtained confirms the non-existence of tricalcium phosphate and the existence of a series of solid

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[10] It has been pointed out (220) that the production of hydroxyapatite from $Ca_4P_2O_9$ by reaction with water in the atmosphere at 1050–1100°C. makes the existence of the latter in aqueous systems improbable.

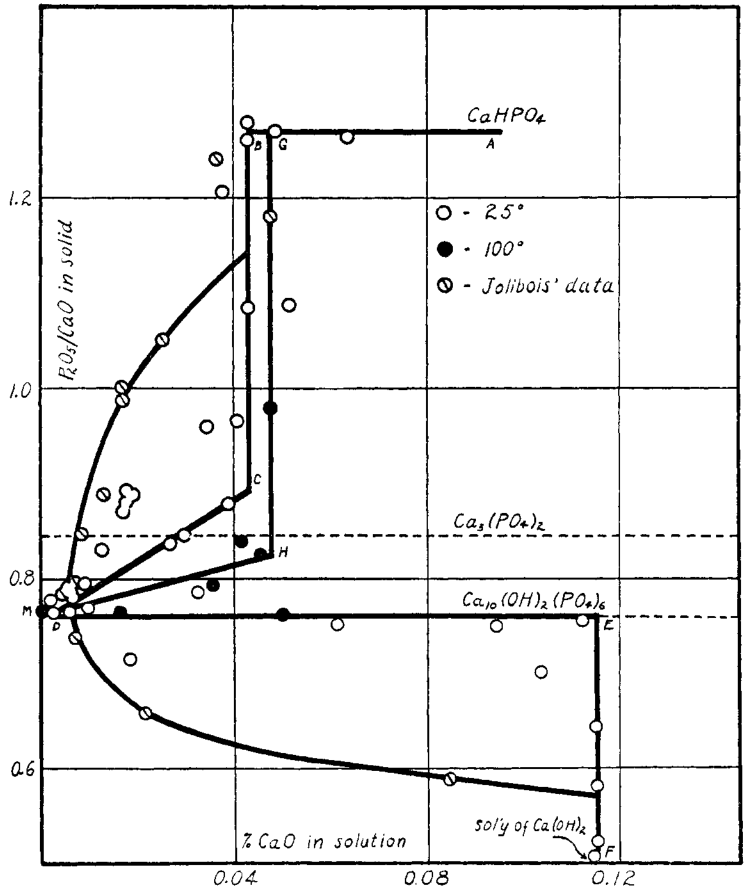

FIG. 4

solutions.[11] But Jolibois' results are different from Bassett's in one important respect: while the series of solid solutions disclosed by Bassett's data ranges in composition from dicalcium phosphate to hydroxyapatite,

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[11] It may also be noted that there is no phase rule foundation for Jolibois' claim to the discovery of a new calcium phosphate. The mole ratios of CaO to P_2O_5 in the four compositions which he assumed to be pentacalcium phosphate varied considerably, while the solutions in contact with these solids had almost constant ratios. Such results are indicative of an invariant system with two solid phases and not of a monovariant system with a single solid phase. Jolibois reports that well-defined crystals may be observed, but furnishes no data on their physical and optical properties. One is forced to conclude that the crystals were probably dicalcium phosphate or pseudomorphs of dicalcium phosphate (12).

that of Jolibois extends to a ratio of P_2O_5 to CaO approximately equal to 0.58, with a solubility minimum at the composition of hydroxyapatite (P_2O_5:CaO = 0.76).

In either case, there is only one composition which is not decomposed by water.[12] The only solution which contains P_2O_5 and CaO in the same proportion as is found in the solid phase in equilibrium with it is located somewhere in the circle in figure 5. Solids with larger ratios of P_2O_5 to CaO will become richer in CaO when treated with water (12, 31, 36, 37,

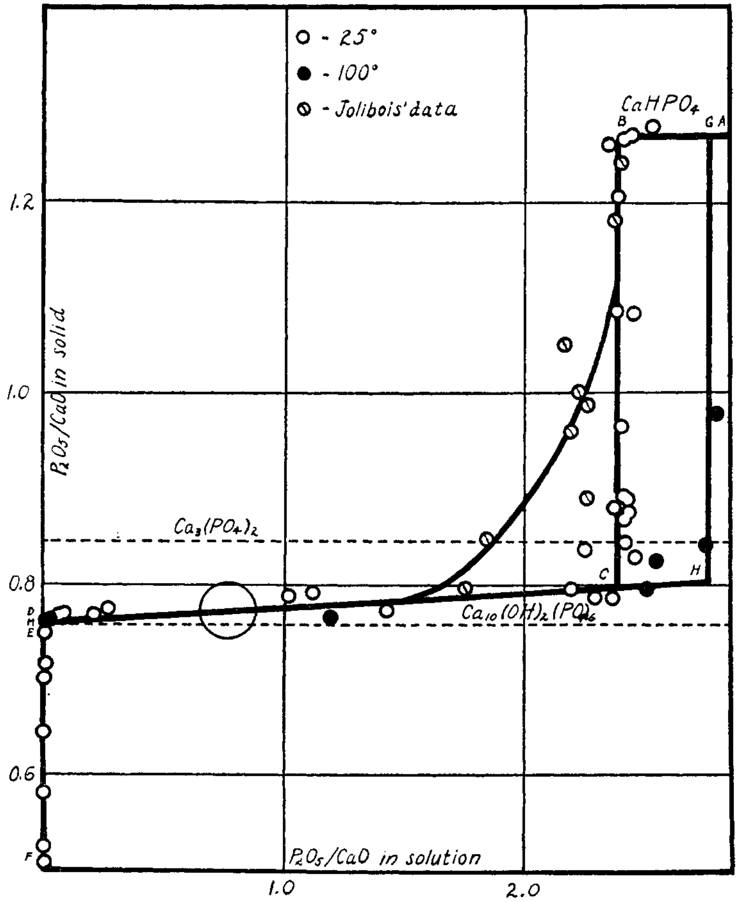

FIG. 5

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[12] Bassett's method of graphing results enabled him to demonstrate that mono-, di-, and tri-calcium phosphates were all incongruently soluble and that hydroxyapatite was the only calcium phosphate which was not decomposed by water. This

38, 40, 53, 57, 171, 183, 184, 186, 223),[13] while those with smaller ratios will become richer in P_2O_5 under similar treatment (18, 162). That hydrolysis proceeds in this manner has been completely verified by Schleede *et al.* (191). They found that all of the calcium phosphates will eventually display x-ray diffraction patterns similar to hydroxyapatite on protracted treatment with water. In addition, $Ca_4P_2O_9$ was the only one which gave alkaline solutions. In the face of this evidence, the following statements appearing in the literature must be incorrect: tricalcium phosphate hydrolyzes to $Ca_4P_2O_9$ (55); $Ca_4P_2O_9$ hydrolyzes to dicalcium phosphate and calcium hydroxide, and all phosphatic materials end as dicalcium phosphate on hydrolysis (227).

The chief uncertainty thus seems to be whether or not hydroxyapatite has a range of existence as a definite compound. The conception of an extended range of solid solutions suggested by Jolibois' data (but not by Jolibois himself) seems to furnish a more consistent explanation for the information available in the literature than does the assumption of a definite molecular species with the formula $Ca_{10}(OH)_2(PO_4)_6$.

For example, calcium phosphates with CaO contents in excess of the amount calculated for $Ca_{10}(OH)_2(PO_4)_6$ have been obtained by the following methods:

(*1*) Addition of limewater to dilute solutions of orthophosphoric acid. When Blarez (18) added excess quantities of limewater, he found that all of the precipitates had a mole ratio of CaO to P_2O_5 in excess of 3 and in some cases in excess of 3.3. Furthermore, all of the precipitates tended toward a composition of 3.6 moles of CaO per mole of P_2O_5 when allowed to stand in contact with their mother liquors whether they contained more or less than this amount immediately after precipitation.[14]

(*2*) Addition of solutions of calcium chloride to dilute alkaline solutions of sodium and potassium phosphates. Blarez reports results similar to those obtained when limewater and phosphoric acid were added. All of the precipitates approached a CaO content of 3.3 moles per mole of P_2O_5 when thoroughly washed with water.

(*3*) Extremely rapid mixing of limewater and orthophosphoric acid. The rapid mixing method of Jolibois produced precipitates (101) which approximated tricalcium phosphate in composition immediately after precipitation. However, on standing in contact with the mother liquor

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confirmed the early results of Warington (223), who showed that persistent hydrolysis of precipitates of tricalcium phosphate caused them to approach the composition of hydroxyapatite.

[13] When calcium phosphates are repeatedly treated with neutral ammonium citrate solutions, the composition of the residues will also approach a ratio of P_2O_5 to CaO equal to about 0.76 (89).

[14] Berthelot (17) obtained similar results.

for 48 hr., the mole ratios of CaO to P_2O_5 increased to values between 3.48 and 4.50, depending on the amount of excess limewater used. Fouretier (59) found by means of x-rays that the initial precipitates were always a mixture of dicalcium phosphate and an amorphous solid. The final precipitates, however, always gave apatite patterns.

(*4*) Boiling precipitated tricalcium phosphate with concentrated sodium hydroxide. Foerster (57) obtained residues with 3.3 moles of CaO per mole of P_2O_5 when he used dilute sodium hydroxide, but with concentrated sodium hydroxide the ratio approached a value of 4.

(*5*) Boiling hydroxyapatite, prepared by ignition, with concentrated sodium hydroxide. Foerster also prepared various samples of hydroxyapatite by igniting mixtures of di- or tri-calcium phosphate with appropriate amounts of calcium oxide or calcium carbonate. In accordance with his previous results, these preparations were unaffected by dilute sodium hydroxide but approached a composition of 4 moles of CaO to 1 mole of P_2O_5 in concentrated caustic solutions. Foerster was able to obtain even 5 to 1 ratios by treating $Ca_4P_2O_9$ or Thomas slags with concentrated sodium hydroxide, but these residues probably contained some free lime.

(*6*) Treatment of hydroxyapatite, prepared by hydrolysis with water or dilute sodium hydroxide, with solutions of limewater. Lorah, Tartar, and Wood (132) found that the lime content of the residues increased steadily for a long time and that the amount taken up at any given time depended on the concentration of lime in solution.

In view of the differences in particle size undoubtedly found in these experiments and differences in solution environment, adsorption cannot furnish a complete explanation of the similarity of results (101, 132). It is equally improbable that large amounts of calcium oxide in the solid phase could be due to free lime, since methods 1, 3, and 6 would then indicate that the solubility of lime is materially lowered in the presence of hydroxyapatite. That this is not so may be seen in figure 4, where it is apparent that mixtures of hydroxyapatite and free lime are in equilibrium with solutions having the same concentration of calcium oxide as saturated limewater. Only one conclusion remains:—solid solutions with more CaO than $Ca_{10}(OH)_2(PO_4)_6$ have a stable existence in contact with solutions of varying concentrations (102). Blarez's results (18) are particularly striking. While he did not achieve equilibrium, it is obvious that he approached a condition of equilibrium from opposite directions.

B. The phase diagram for calcium arsenates

The phase diagram for calcium arsenates has been the subject of some recent studies. The evidence is briefly presented because of the similarities between the phosphates and the arsenates.

The results obtained by Pearce and Norton (163) for the 90°C. isotherm are plotted in figure 6 on an enlarged scale. It will be noted that penta- and tri-calcium arsenates, as well as the analog of hydroxyapatite, are assumed to exist. A similar type of curve is reported for 35°C. (164), but no evidence is found for the basic compound and the ranges of equilibrium concentrations in solution are somewhat different.

The method used was ingenious. It consisted of arranging the concentrations of CaO and As_2O_5 in the solution so that when the temperature was raised to the desired level only a small amount of solid would precipitate (calcium arsenates are less soluble at higher temperatures). If the separation of the solid could take place with little disturbance to conditions in solution, the initial precipitate would be so near to its final composition that equilibrium would be reached in a very short time.

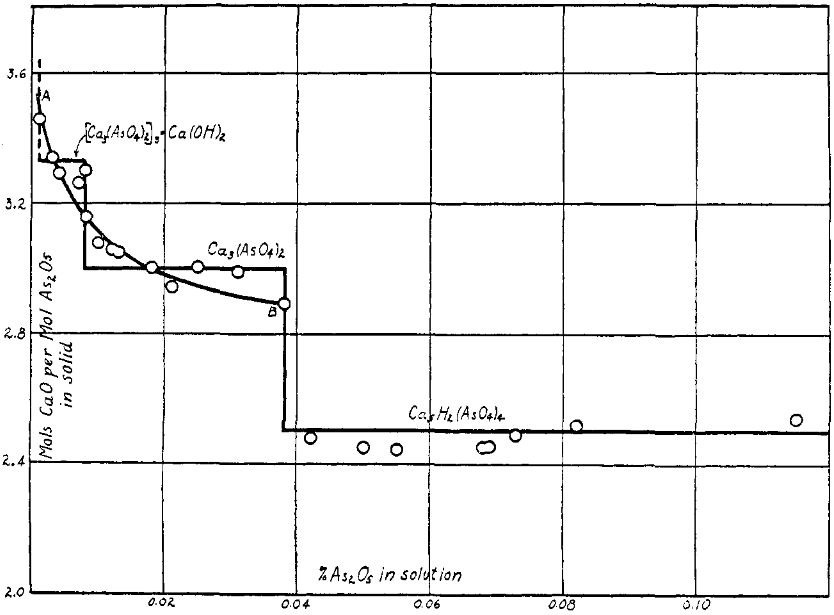

FIG. 6

However, if the ratios of CaO to As_2O_5 in the solutions before and after precipitation are calculated from the data of Pearce and Norton, it is found that while the change in this ratio is generally of the order of 10 per cent, several of the most basic compositions show a much larger change,—up to 700 per cent.

It may be assumed, therefore, that the method used did not yield equilibrium conditions in the most basic region. That the curve reported by Pearce and Norton for this region is probably incorrect, is shown by the fact that it was necessary for them to assume that one of the preparations consisted of a mixture of the basic compound and free lime. It would be surprising if precipitation from limewater produced an equilibrium with free lime in the solid phase. The curve *AB* in figure 6 has been drawn to represent a series of solid solutions. It may be seen that it fits the data at least as well as the curve drawn by the original authors, and the point which originally was taken to indicate a mixture of basic arsenate and lime in the solid phase now has a more reasonable significance.

A more recent publication (156), in which x-ray and petrographic methods were used to determine the 62°C. isotherm, confirms the existence of a solid solution in the basic region. Some effort was made to determine the extent of solid solution on the high-lime side but it appears, unfortunately, that the limiting composition on the low-lime side was assumed to be tricalcium arsenate. The existence of pentacalcium arsenate, reported by Pearce and his associates, has also been confirmed by Nelson and Haring and seems to rest on much sounder evidence than does the existence of pentacalcium phosphate. The hydrolysis of the calcium arsenates follows much the same course as does that of the calcium phosphates.

C. The nature of precipitated basic calcium phosphate

Attention has been concentrated thus far mainly on evidence susceptible to phase rule treatment. However, because of the practical difficulties inherent in phase rule procedures, many investigators have turned to x-ray diffraction methods. But despite the fundamental character of such research, a number of different conclusions have been proposed.

Trömel and Möller (220) found that a number of precipitates of different composition gave x-ray patterns identical with that of hydroxyapatite.[15] Since they could detect no change in lattice dimensions as the composition varied, they concluded that precipitated tricalcium phosphate was essentially hydroxyapatite with sufficient adsorbed phosphate to yield the proper composition and not an hydrato-apatite, $Ca_9(H_2O)_2(PO_4)_6$, as proposed by Hendricks *et al.* (74).[16]

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[15] Precipitation in boiling solutions improved the sharpness of the lines in the x-ray photographs. Trömel and Möller took this as an indication of growth in particle size. An alternative explanation,—one which many x-ray workers ignore and which is very applicable to this field,—is a growth in uniformity of composition among the various particles. If particles differing in composition but all having an apatite lattice are present, the small differences in lattice dimensions will cause the lines to lose sharpness.

[16] Hendricks *et al.* believed that this hydrato-apatite could be distinguished from other apatites by the disappearance of the apatite pattern on ignition. From the discussion in the section on the binary system, it is evident that this is not strictly

Trömel and Möller made much of the fact that the composition of the precipitate when the calcium solution was poured into the phosphate solution was different from the composition when the order of mixing was reversed (66, 127). They believed that in the former case an opportunity for adsorption is offered and accepted. However, it has been amply demonstrated that initial precipitates of basic calcium phosphates require much time to change over to their equilibrium compositions (page 258). Moreover, it has already been pointed out that adsorption cannot furnish a complete explanation for such phenomena (page 270).

The failure to obtain any noticeable differences in the x-ray patterns of widely varying compositions is probably due to the smallness of the change in lattice constants and insufficient precision in x-ray methods. That this is plausible is shown by the fact that Bredig *et al.* (25) have prepared a calcium aluminate- and a calcium ferrite-apatite which cannot be distinguished from fluoro-apatite by x-rays. It is to be expected, however, that with recent improvements in precision (45, 46, 47, 222) such slight differences will become measurable.

Bredig *et al.* (25) offered an entirely different concept to explain the continued appearance of apatite patterns as the composition was varied,—the formation of mixed apatites (apparently what was meant was something like double or multiple salts). They were able to show that $Ca_4P_2O_9$ could be transformed into an apatite at high temperatures by the absorption of water in quantities much less than the stoichiometric amount for hydroxyapatite. They approached the same result from the opposite direction by removing part of the water from hydroxyapatite. The product was considered to be a mixed hydroxy-oxy apatite. In a similar manner, a mixed fluoro-oxy apatite was synthesized by absorption of small quantities of calcium fluoride under conditions eliminating the effect of moisture. The existence of other so-called mixed apatites was postulated, and Bredig *et al.* were very successful in explaining certain anomalous phenomena with them.

All of the foregoing authors recognized inadequacies in their hypotheses. Hendricks *et al.* (74) concluded, "For structural reasons such a compound (hydrato-apatite) would be expected to form a complete series of solid solutions with hydroxyapatite . . ." Trömel and Möller (220) suggested the possibility of the formation of mixed crystals (presumably synonymous with solid solutions) of hydroxyapatite and hydrated tricalcium phosphate.

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so, since any hydroxyapatite will lose the apatite pattern if ignited in the absence of moisture. The same may also be true of the so-called carbonate–apatites. Others have shown that precipitated tricalcium phosphate can have an apatite pattern or the pattern of either of the anhydrous tricalcium phosphates, depending on the temperature of drying (24, 220).

Bredig *et al.* (25) thought it probable that precipitated tricalcium phosphate was composed of mixed crystals of hydrated tricalcium phosphate (in which the water does not necessarily follow any stoichiometric relationship) and hydroxyapatite (with or without adsorbed phosphate according to circumstances), but their final conclusion was that it is not yet possible to come to any definite decision. The essential difficulty seems to be a certain reluctance to abandon the idea of discrete molecular types among the apatites.

The results of this unwillingness to accept the idea of a crystal lattice existing without discrete molecular types are also illustrated by the work of Roseberry, Hastings, and Morse (178). They came to the conclusion that tricalcium phosphate may exist as a definite, independent crystal form. And yet they felt it necessary to suggest that this crystal form appears to be the nucleus of the apatite series. When CaX_2 is associated with tricalcium phosphate, its molecules are placed in the crystal lattice where they cause no detectable difference in the important planes. They believed that tricalcium phosphate is not as stable a form as $CaX_2 \cdot nCa_3(PO_4)_2$, where $X = Cl$, F, $\frac{1}{2}O$, or $\frac{1}{2}CO_3$ and n is not less than 2 nor more than 3.

Larson (126) has more recently proposed a monohydrate formula, $Ca_3(PO_4)_2 \cdot H_2O$, for precipitated tricalcium phosphate. The evidence is not convincing. The x-ray patterns for the freshly precipitated substance and its product of ignition are reported to be different from the oxy- and hydroxy-apatite patterns of Trömel (217). This is undoubtedly true for the ignited salt, which should give the pattern for β-tricalcium phosphate. The failure to obtain or to recognize an apatite pattern for the un-ignited material is probably due to the generally unsatisfactory nature of the basic precipitates for x-ray powder work when freshly precipitated. The remaining evidence is the loss of 0.97 mole of water on ignition at 950–970°C.

D. Reaction rates

Figure 7 is reproduced from a paper by Buch (31), who extended Rindell's work on the hydrolysis of dicalcium phosphate. Rindell (172) states that equilibrium is not attained in some cases in 252 hr. Schleede *et al.* (191) also report that $CaHPO_4 \cdot 2H_2O$, agitated for 80 hr. with constantly renewed hot water, gave x-ray patterns of $CaHPO_4$ and did not show the apatite pattern until after 400 hr. of hydrolysis. It is obvious, therefore, that the 20-hr. extractions on which figure 7 is based did not give equilibrium conditions and do not prove, as Buch thought, that compounds exist with compositions between those of dicalcium and tricalcium phosphates.

Buch's results are significant, nevertheless, in that they lead to some idea of reaction rates. From figure 7 it would seem that the rate of hydrolysis of a mixture of dicalcium phosphate and solid solution decreases until a critical proportion of the latter is present. Sanfourche and Henry (184) found that a small quantity of "tricalcium phosphate" was necessary to induce dicalcium phosphate to hydrolyze. With the critical quantity of solid solution present, the rate rises rapidly and remains fairly constant until the dibasic salt is no longer present. Buch states that his residues did not become completely amorphous (indicating complete disappearance of dicalcium phosphate) until just before the sharp drop from the upper plateau in figure 7. The rate of reaction from then on is extremely slow and decreases as the residue becomes richer in calcium oxide.

It is instructive to determine the results which Buch and Rindell should have obtained had they been able to reach equilibrium in their extractions. In figure 8 point *A* represents pure dicalcium phosphate. On treatment with water, the solution will contain relatively more phosphate than the original solid. Hence at equilibrium, represented by point *B*, the solid will have proportionately more calcium oxide. Separation of the solid from the solution brings the system to point *C*. A second extraction ends at point *D*, which represents a solid phase in equilibrium with a solution of the same composition as the one which was in equilibrium with solid B. Thus, as long as dicalcium phosphate persists in the solid phase, the composition of the solution after each extraction will remain constant. This is illustrated by *BD* in figure 9. However, as soon as the system becomes monovariant, each successive solution will display continuously decreasing ratios of P_2O_5 to CaO, until finally at *E* the proportion becomes equal to that found in the solid. At this point

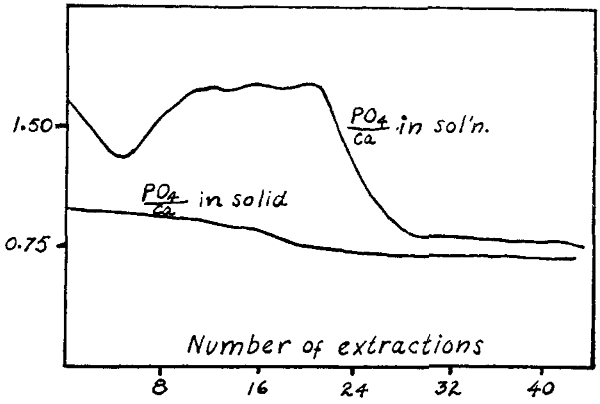

FIG. 7

the solid ceases to become richer in calcium oxide and all succeeding solutions will have identical compositions.

III. THE STABILITY OF THE APATITE LATTICE

The apatite lattice is tolerant not only to large variations in the components of the ternary system CaO–P_2O_5–H_2O, but also to the inclusion of many other substances in large or small amounts. From the evidence which is about to be examined, one is inevitably forced to the conclusion, already stated for the ternary system, that *it is only a fortuitous occurrence when the composition of any apatite may be expressed by small whole number ratios of atomic species suggesting a definite chemical compound.*

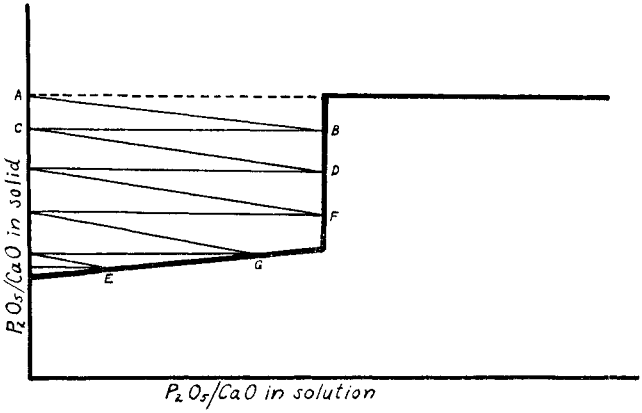

FIG. 8

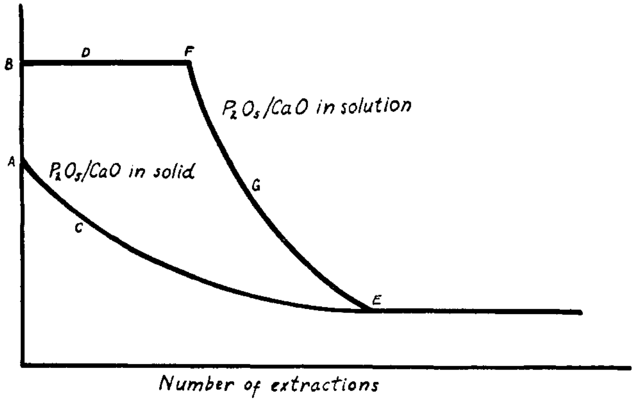

FIG. 9

A. *Mineralogical studies*

Schleede *et al.* (191) have stated, "According to the lattice determinations of Schiebold and Mehmel (147) and of Náray-Szabó (181), relatively large spaces are available for fluorine atoms or hydroxyl groups .... As a result ... still larger units such as Cl (155), CO_3 (23, 56), or SO_4 (23, 56) may be built in. It does not appear excluded, then, that a still larger number of molecules of water besides the two hydroxy groups can be placed in the space provided."[17, 18]

The most revealing investigations of apatite minerals are those of McConnell and his associates (68, 69, 144, 145, 146). On the basis of x-ray studies of carefully prepared and carefully analyzed[19] samples, the following conclusion was reached (69): "Each unit cell (of fluorapatite) possesses the following types of ionic positions: 24 O, a few of which may be occupied by OH or F ions, if an excess of either should be present; all of the O ions are bonded to P ions; 2 F, which may be entirely, or in part, occupied by OH, Cl, or O ions; 6 P, a small number of these positions,

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[17] Our translation.

[18] The structures proposed by Mehmel and by St. Náray-Szabó have been reproduced several times (68, 69, 74, 145). Lattice dimensions are given in the following table:

	a_0	c_0	c/a	VOLUME	DENSITY BASED ON MOLECULAR WEIGHT OF 1008.9
	Å.	Å.		cu. Å.	
Fluoro-apatite (145)	9.36 ±0.01	6.88 ±0.01	0.7350	522	3.187
Fluoro-apatite (181)	9.37 ±0.01	6.88 ±0.01	0.7342	523	3.180
Fluoro-apatite (147)	9.36 ±0.02	6.85 ±0.02	0.7318	520	3.201
Francolite (68)	9.34 ±0.01	6.88 ±0.01	0.7366		
Dahllite (69)	9.41	6.88	0.7311	528	
Enamel (69)	9.41	6.87	0.7301	527	3.055
Dentine (69)	9.40	6.87	0.7309	526	3.024
Hydroxyapatite (34)	9.42	6.94	0.736	533	
Hydroxyapatite (116)	9.40	6.93	0.737		
Chloro-apatite (116)	9.52	6.85(?)	0.719		
Lead hydroxyapatite (116)	9.90	7.29	0.736		
Pyromorphite (116), $Pb_{10}Cl_2(PO_4)_6$	9.95	7.32	0.736		

Optical properties of apatite minerals have been published by others (3, 52).

[19] McConnell has pointed out that much of the previous work is unreliable for crystallographic analyses because of the difficulty in securing accurate chemical analyses. This is substantiated by the scheme worked out by Harvey (71) for the complete analysis of apatite rock.

probably not exceeding 10 per cent, may be occupied by C, V, or As; Si and S may also occupy these positions; 10 Ca, a small amount of Ca may be replaced by C, in which case all of the ten positions are not necessarily filled, because C can replace more than one Ca, depending upon the number of charges required to produce electrostatic equilibrium." In addition to these isomorphous substitutions, the following were also suggested (145): for calcium,—magnesium, manganese, strontium, sodium, potassium, and possibly barium, chromium, iron, aluminum, cerium, and other rare earths.[20] Where oxygen substitutes for fluorine, either (*a*) part of the calcium is replaced by a trivalent metal, or carbon, or possibly nitrogen; or (*b*) part of the phosphorus is replaced by a hexavalent ion such as sulfur.

Other chemical, optical, and x-ray studies of phosphatic minerals have established the fact that the apatite lattice is capable of enduring very wide variations in composition (21, 74, 75, 174, 175, 176, 189, 190, 207).[21]

B. Basic phosphates of other metals

Klement (116) has recently discovered some remarkable similarities between the basic regions of the ternary systems $CaO-P_2O_5-H_2O$ and $PbO-P_2O_5-H_2O$. For example, the final product of the hydrolysis of dilead phosphate is the analog of hydroxyapatite. It is asserted, moreover, that lead hydroxyapatite is the only basic lead phosphate stable in water.

Klement (115) has also made a thorough investigation of the basic phosphates of magnesium. Although dimagnesium phosphate does not hydrolyze in the same way as dicalcium phosphate, compositions such as $Mg_{10}(OH)_2(PO_4)_6 \cdot 27H_2O$ can be obtained by hydrolysis in pure water. Since this substance is monoclinic instead of hexagonal, it is not an apatite. Klement's data suggests the possibility that a continuous series of solid solutions also exists in this system.

Sanfourche (185) believes that strontium forms an analog of hydroxyapatite but that barium does not. This conclusion is based on certain similarities in behavior when the alkaline-earth hydroxides are titrated with phosphoric acid and should be regarded as tentative until additional information is obtained.

Jolibois and Cloutier (102), using the former's rapid mixing method, have concluded that the basic phosphates of lead, copper, iron, aluminum, zinc, silver, manganese, chromium, and uranium probably do not exist. This conclusion is also in need of confirmatory evidence, especially since it has already been shown to be wrong with respect to lead.

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[20] Körber and Trömel (119) have prepared an apatite compound with the formula $La_2Ca_8(PO_4)_6 \cdot O_2$.

[21] For detailed optical properties and a bibliography up to 1929, see Hausen (73).

PART II. PRACTICAL APPLICATIONS

Enough is now known of the aqueous calcium phosphate system so that one can begin to understand materials and processes of great practical importance. However, a word of caution is necessary at the very beginning. It has not been easy to learn what we know of the system $CaO-P_2O_5-H_2O$, and it is by no means certain that our knowledge is complete or correct in all of its details. But the soil, mineral, and biological systems which are the subjects under consideration in this section are infinitely more complex in their relationships, and therefore our knowledge of them is much less reliable. It is unfortunate that many workers in these fields have given insufficient consideration to the difficulties of applying the simple things that can be done in the laboratory to complicated natural phenomena. The conclusions, which have been reached on a foundation in which many factors, some of controlling importance, have been ignored, are rash and have tended to distract attention from much good data. It is obvious, therefore, that much of what is stated here is of the nature of a first approximation and more dependable knowledge waits upon future work.

Natural processes are dynamic, and information based on studies of equilibrium conditions is necessarily of limited usefulness. It is doubtful that we shall get very far with investigations of soil reactions or bone deposition merely with what is known of ionic equilibria, solubility product, or simple phase rule systems. Future work should emphasize investigations into phenomena in flux rather than systems in their final states. Only then will our present knowledge achieve its maximum usefulness.

I. PHOSPHATIC FERTILIZERS

Since this review is confined to the basic calcium phosphates, the manufacture and composition of superphosphate or triple superphosphate will not be presented here. However, attention should be drawn to the excellent paper of Hill and Hendricks (77), in which a combination of chemical, optical, and x-ray methods has been used to determine the composition of these materials. For economic information, see Jacob's reports (93).

A. Calcined phosphate

The availability of $Ca_4P_2O_9$ for plant food has long been known, but it was not until comparatively recently that α-$Ca_3(PO_4)_2$ was also shown to be highly available (25, 91, 215). It follows then from the discussion of the binary system $CaO-P_2O_5$, that if fluorine could be removed from phosphate rock, the phosphate content could be made available by a simple ignition at 1200°C. or higher, followed by rapid cooling, or by cooling in a dry atmosphere. Providing that the presence of silica has no marked effect, such a procedure should produce a mixture of α-$Ca_3(PO_4)_2$ and $Ca_4P_2O_9$ from most phosphate rocks.

The major problems are (*a*) how to remove fluorine, as the presence of fluorine has a marked effect in rendering phosphatic materials unavailable (4, 5, 10, 25, 104, 120, 134, 180); (*b*) how to prevent or minimize the formation of hydroxyapatite through reaction with atmospheric moisture during cooling; (*c*) how to prevent or minimize the transformation of α-tricalcium phosphate to the less soluble β-tricalcium phosphate during cooling. The Bureau of Chemistry and Soils of the United States Department of Agriculture made a systematic effort to solve these problems, and the results are contained in a series of papers which are remarkable for their thoroughness and soundness (95, 142, 166, 167, 168).

The problem of removing fluorine was solved by high-temperature ignitions in the presence of (*a*) steam and silica, or (*b*) water vapor alone, or (*c*) silica alone with the effectiveness varying in the order given. There was no significant increase in citrate-solubility at any temperature until all the fluorine had been removed except the amount theoretically required for the formula $Ca_{10}(OH)(F)(PO_4)_6$. In fact, the removal of less than 65 per cent of the fluorine generally caused a decrease in citrate-solubility, confirming an earlier observation of Bredig *et al.* (25) that fluoro-oxyapatite had a smaller citrate-solubility than fluoro-apatite. After the removal of 65 per cent of the fluorine, the citrate-solubility depended jointly on the amount of fluorine further volatilized and the temperature. If the volatilization was carried out at 1350°C. or higher, or if the temperature is subsequently raised to that level, the increase in citrate-solubility was roughly proportional to the amount of fluorine further removed. Once the fluorine was volatilized,—and this could be done at comparatively lower temperatures,—the ignition temperature was the controlling factor, in that before the charge was chilled a temperature of at least 1350°C. had to be attained.

It was found that if the furnace was cooled slowly to 1300°C. and then the charges chilled by withdrawal from the furnace, no significant decrease in availability occurred. However, if slow cooling was continued to temperatures lower than 1200°C., the decrease in availability was large. If in the latter case the annealing was performed in a dry atmosphere, the decrease in citrate-solubility was materially lessened although it was still considerable.

By means of a carefully planned series of experiments, it was shown that the presence of silica is beneficial for the conversion of most varieties of synthetic and natural phosphates to forms available for plant food. This is not unexpected, since Körber and Trömel (119, 120) have shown that, in the system CaO–P_2O_5–SiO_2, α-$Ca_3(PO_4)_2$ and $Ca_4P_2O_9$ have extended ranges of homogeneity and the velocity and temperature of the transformation of α-tricalcium phosphate to β-tricalcium phosphate are considerably reduced. Furthermore, if silicophosphates are formed, their P_2O_5 contents are highly available.

Marshall *et al.* (142) have suggested the following mechanism for the calcining process: (*a*) one atom of fluorine from fluoro-apatite is replaced by hydroxyl, yielding hydroxyfluoro-apatite which is very insoluble in neutral ammonium citrate; (*b*) the second atom of fluorine is replaced by hydroxyl, yielding hydroxyapatite which also has a low citrate-solubility; (*c*) hydroxyapatite decomposes. Water vapor and silica are necessary for the first two steps. Water interferes with the third step unless silica is present.[22]

Subsequent x-ray investigations (78, 143) disclose that the rôle played by silica is not a simple one and that reversion, or decrease in availability, involves several complex phase transformations.

While the desirable effects of dry annealing over wet annealing were, in general, confirmed, marked variations were found and seem to be due to variable composition. The transformation of α-$Ca_3(PO_4)_2$ to the beta variety does not take place and hence cannot account for reversion. However, reversion was always accompanied by the appearance of apatite and is almost certainly due solely to the formation of apatite. The evidence seems to indicate that two different apatites are produced, one which requires the presence of moisture and one which does not. The latter forms at a higher temperature and usually has a greater effect on citrate-insolubility. Contrary to expectations, the presence of $Ca_4P_2O_9$ was not reported. While α-$Ca_3(PO_4)_2$ is usually the dominant phase in the unreverted samples, silicocarnotite and one or more phases of unknown composition may also occur.

The advantages of calcined phosphate over superphosphate have been summed up (142) as follows: (*a*) the product is a sintered or semi-fused clinker requiring no aging, merely grinding; (*b*) the product is practically insoluble in water and gives weakly alkaline solutions, thereby avoiding bad effects on machinery and fertilizer bags, although possibly leading to loss of ammonia when mixed with ammonium salts (13); (*c*) the product contains about 30 per cent available P_2O_5 as compared with 19 to 20 per cent in the best grades of superphosphate (transportation cost is a considerable item in the total cost to the consumer (48)); (*d*) the product has superior mechanical condition alone and in mixtures (226); (*e*) pot tests (30, 94, 179, 198) show plant food values as high as superphosphate or dicalcium phosphate; (*f*) low fluorine content creates the possibility of

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[22] Messerschmitt (148) believes that the silica combines with any excess calcium, thus preventing the formation of apatite.

substitution for bone meal in mineral feeds for livestock. The process cannot be used for phosphate rocks rich in iron or aluminum phosphate, since these are rendered almost completely unavailable by calcination.

An effort at commercial development (48) has, however, uncovered the following practical difficulties: (*a*) the temperature required is just below the fusion temperature and incipient fusion leads to problems of handling; (*b*) phosphate rocks vary considerably in composition, producing varying fusion temperatures, and therefore close temperature control becomes necessary. A good product was obtained by fusing the rock and bubbling in dry steam. The objections to this procedure were low refractory life[23] and high fuel costs. These obstacles seem to have been overcome by the St. Jacques turbulent furnace (182), in which the fine particles of rock are suspended in a gas stream during the reaction period. A commercial plant based on the use of this furnace has been constructed in Algeria.

Until recently, the calcining process seemed destined to play an important part in the phosphate fertilizer industry (93, 229). It may still do so in other countries, but in the United States there has been a sharp drop in interest. This is probably due to the remarkable results reported by the Tennessee Valley Authority on calcium metaphosphate (50, 135), which contains better than 60 per cent available P_2O_5. Here may be an example of a very promising process becoming obsolete even before it could be placed into large-scale production. It would be particularly striking to find such an example in this industry, in which technological progress has lagged so far behind.[24]

B. Thomas meal

If the discussion on calcined phosphates is broadened to include mixtures richer in lime and silica, then the basic slags of the steel industry become included. Tetracalcium phosphate and one or more silicophosphates are the important sources of available P_2O_5 in these slags (4, 120, 194).

The compositions of the silicophosphates are still uncertain. The following formulas have been proposed: (*a*) $5CaO \cdot P_2O_5 \cdot SiO_2$ (4, 14, 19, 24, 119, 120, 124, 191, 193) (silicocarnotite); (*b*) $9CaO \cdot P_2O_5 \cdot 3SiO_2$ (119, 120); (*c*) $8CaO \cdot P_2O_5 \cdot 2.5SiO_2$ (157); (*d*) $7CaO \cdot P_2O_5 \cdot 2SiO_2$ (157); (*e*) $10CaO \cdot 3P_2O_5 \cdot SiO_2$ (57); (*f*) $3CaO \cdot P_2O_5 \cdot 3SiO_2$ (161); (*g*) $13CaO \cdot 3P_2O_5 \cdot SiO_2$ (124). Formulas *e* and *g* are not supported by adequate experimental data and *f* has been ruled out by x-ray examinations (24). Compositions *b*, *c*, and *d* have identical diffraction patterns and are thus one and the same com-

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[23] For results on commercial operation of phosphate-smelting furnaces, see reports by the Tennessee Valley Authority (No. 51,160).

[24] Problems connected with analyses of calcined phosphate have been worked out by Jacob and his associates (96, 179).

pound. It may be said then that only two ternary compounds have been discovered in the system $CaO-P_2O_5-SiO_2$. And only on the formula of silicocarnotite has there been any general agreement. The readiness with which solid solutions are formed has much to do with the difficulty in determining the compositions of the various compounds in this system (119).

Much of what has been said of calcined phosphate may be applied to Thomas meal. As far back as 1892, Foerster (57) observed that a large portion of the P_2O_5 in $Ca_4P_2O_9$ became unavailable on annealing at moderately high temperatures. He very shrewdly ascribed the effect partly to temperature transformation and partly to reaction with constituents in the atmosphere. On these assumptions he recommended that basic slags be cooled rapidly,—a bit of advice which has been repeated more recently (104, 191).

Fluorine in basic slags is just as objectionable as fluorine in calcined phosphates. Thus, efforts to increase the amount of fertilizer by-product by adding raw phosphate rock to molten slags have failed because of the effect of the fluorine in the added material on the availability of the P_2O_5 (120).

II. REMOVAL OF FLUORIDE ION FROM WATER

The stability of the apatite lattice to a large variety of isomorphous replacements creates the possibility of developing a number of useful ion-exchange reactions.

The recognition of fluorine as the cause of the disease known as "mottled teeth" has stimulated the development of processes for removing small quantities of fluorides from potable waters. Several recent proposals are based on the use of calcium phosphates. The usefulness of such compounds is undoubtedly due to the ability of fluoride ion to replace hydroxyl ion in the apatite lattice.

The removal of solute fluoride by the formation of fluoro-apatite was apparently first noted by MacIntire and his associates (133, 134). The first actual attempt to develop a practical process seems to have been made by Smith and Smith (208), who used ground bone as the source of replaceable hydroxyl ion.

MacIntire and Hammond (136) have shown that almost any method whereby hydroxyapatite is produced in the water to be purified[25] is effective. For economic reasons, however, it is better to have the water flow through towers packed with the active substance and to devise a method for regenerating exhausted material.

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[25] For example, baking powder suspensions made alkaline with ammonia or calcium hydroxide.

The replacement of OH^- by F^- is easily reversed by washing with dilute sodium hydroxide, but the subsequent removal of excess alkali was not so easy. A water wash followed by a wash with dilute hydrochloric acid was found to be effective (2, 208) but was open to the following objections (15): metal corrosion; loss of phosphate; and an effective life of only about twenty-five cycles. These difficulties were overcome by substituting a water solution of carbon dioxide for the hydrochloric acid (15).

Patent protection for these processes has been sought (2, 15, 230).

III. THE INORGANIC CONSTITUENTS OF BONE[26]

Although the idea of isomorphous replacement in the apatite lattice has already been tentatively proposed in connection with the nature of the inorganic constituents of bone (6, 178, 211), it has made surprisingly little headway. Now that Gruner *et al.* (69) have published a detailed study of the apatite lattice in teeth, giving an exact description of the various possibilities of isomorphous substitution, there should be little excuse for retaining certain outworn conceptions. It is hoped that the weight of evidence here assembled will stimulate a general reorientation on the problem of bone deposition.

X-ray studies have established beyond any question the apatite nature of the salts of bones and teeth (6, 7, 8, 25, 26, 43, 69, 74, 103, 110, 111, 112, 117, 150, 151, 169, 170, 178, 188, 211, 212, 213, 214).

Marek, Wellman, and Urbányi (137, 138, 139, 140, 141) discounted x-ray evidence on the ground that conflicting conclusions had been reached. They failed to recognize, however, that whatever other disagreements x-ray investigators have had, they all agree that the crystallites in bones and teeth are apatites of one kind or another. The only exception is Funaoka (62), who noted the similarity between the x-ray patterns of bones and precipitated tricalcium phosphate but was not aware that the latter was an apatite.

Marek *et al.* also pointed out that the crystal structure of the samples used for x-ray analyses have been so altered by chemical or thermal treatment as to render them no longer representative of the original bone or tooth substance. It is true that many investigators have ignored the possibility that essential changes might occur when bones are ignited or subjected to the action of a glycerol solution of potassium hydroxide,—both common methods for removing organic matter. When Marek and his associates demonstrated (139) that the usual wet methods for isolating pure mineral constituents produce modifications in composition, they

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[26] For information on bony structures as a whole and an excellent bibliography, consult Huggins' review (88). Reviews are available for other aspects of calcification (173, 192).

emphasized the dangers of such neglect. But, on the other hand, it is also true that much evidence has been produced for which this criticism is not valid. Apatite patterns have been reported for a large variety of animal and human bones, teeth, and pathological calcification where the samples have been untreated or have been freed of their organic matter by methods which do not appear to have any effect on the essential inorganic structure (26, 74, 169, 178, 211).

It should be clear, therefore, that any attempt to resolve the contradictory views on the nature of the mineral constituents of bone must be limited to apatite structures.

Since "... the crystalline constitution of enamel and dentine (and bones) is not entirely uniform and may vary considerably from person to person, and even from one part of the tooth to another, and still not be perceptible in appearance or even in such crystal diffraction photographs as have hitherto been made" (6), the chemical evidence must be examined to determine whether or not particular apatites are present in bones and teeth (111, 213).[27]

A. *Carbonate–apatite versus hydroxyapatite*

Werner and others (32, 33, 64, 205, 225) came to the conclusion that carbonate–apatite is the principal inorganic constituent of bone, because bone analyses often approximated the proper proportions of calcium, phosphate, and carbonate. Others have shown that the carbonate content of bone cannot be due to the presence of free calcium carbonate.

Gassmann (64) pointed out that calcium carbonate was easily soluble in glacial acetic acid, while the carbonate in bone was not.[28] He (64, 65) also heated bones and teeth with barium chloride and found that chlorine became bound in some insoluble form. He believed that if free calcium carbonate were present, soluble calcium chloride would have been formed.[29]

Hendricks and coworkers (74) heated mixtures of calcium carbonate and "hydrated tricalcium phosphate" or "pure" hydroxyapatite to con-

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[27] Many years before x-rays were known or applied in this field, the composition of bony substances and their chemical behavior led to the assumption that an apatite was present (1, 85, 225). Numerous analyses show an approximately constant mole ratio of $Ca:P = 10:6$ for many kinds of bone under a wide variety of conditions (20, 22, 28, 29, 63, 64, 80, 81, 87, 107, 122, 137, 152, 195, 200, 204, 205, 209, 225).

[28] Klement (108) disputed this finding by showing that calcium carbonate is practically insoluble in anhydrous glacial acetic acid. It must be recognized, however, that whatever reagent Gassmann used, it had a different effect on calcium carbonate than it did on bone.

[29] Klement has remarked (108) that the chlorine could have been rendered insoluble by reaction with hydroxyapatite even if free calcium carbonate were present.

stant weight at 900°C.; in both cases free lime almost equivalent to the added calcium carbonate was formed. Similar treatment of bone samples gave no substantial amount of free lime.

Thus there seems to be little reason to doubt that carbonate in bone is part of the fundamental apatite.[30] The contention of Klement (107, 111, 117) that the absence of a 10:6:1 ratio of calcium, phosphate, and carbonate in saturated solutions of bone proves the absence of carbonate-apatite and that the presence of a comparatively large amount of carbonate in solution (131) proves the presence of hydroxyapatite and the carbonates or bicarbonates of sodium, potassium, and magnesium (12) is without merit. For if complex apatites exist in bone, it is very likely that they are incongruently soluble[31] and can establish equilibria with solutions of widely varying compositions.

However, a great deal of analytical data is available to show that the inorganic constituents of bone cannot be represented by the formula $Ca_{10}(CO_3)(PO_4)_6$.

It has been demonstrated that bone contains more basic equivalents than acid equivalents, leading to the supposition that hydroxyl groups make up the difference (63, 107, 117, 128, 152). Furthermore, the proportion of carbonate is quite variable and seems to depend on definite factors such as age, disease, and species (28, 58, 87, 105, 117, 121, 125, 128, 137, 138, 152, 158, 159, 202). In many cases, after deducting from the total calcium amounts equivalent to the carbonate present, the ratios of residual calcium to phosphorus are greater than the theoretical ratio for tricalcium phosphate and sometimes even exceed the theoretical ratio for hydroxyapatite (121, 152, 202).

Not only is the proportion of carbonate often less than would be expected for $Ca_{10}(CO_3)(PO_4)_6$, but it is occasionally more (121, 202).

Thus, those who consider carbonate-apatite the principal inorganic constituent of bone (64, 65) are no more right than those who support hydroxyapatite for that rôle (118).

B. Minor constituents

Evidence on the forms taken by the minor constituents of bone is comparatively meager and in general inconclusive. There are some reasons

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[30] Henschen, Straumann, and Bucher (76) have reported lines for calcium carbonate in x-ray spectrograms of bone, but their results have never been duplicated by any of the other x-ray investigators.

[31] The term "incongruently soluble" is usually applied to a compound which is partially or completely changed to another compound in the process of forming a saturated solution. It is used here to signify any change in solid phase, especially the formation of a solid solution of different composition, caused by the fact that no equilibrium exists between a given solid and a solution of identical solute composition.

for believing, however, that magnesium, alkali metals, chlorine, and fluorine are part of the main apatite crystal.

As far back as 1872, Aeby (1) suggested that fluorine occurs as a substitute for oxygen in oxyapatite, since varying amounts had little, if any, effect on the relative proportions of calcium and phosphorus. The fluorine content is variable within a considerable range but is always much less than the theoretical for fluoro-apatite (22, 63, 97, 98, 105, 106, 110, 113, 114, 117, 199, 216). The minerals in fossil bone usually contain increased amounts of fluorine (42, 165, 175, 176, 177), which appear to enter the lattice by isomorphous replacement of CO_3 and H_2O (74) or OH (114).

Analytical results form the basis of several attempts to account for magnesium and the alkali metals as carbonates or bicarbonates (12, 107, 110, 111, 117). These attempts fail for many bone compositions (138, 139, 154). Moreover, Logan (128) makes the pertinent observations that alkali metals, which do not form insoluble phosphates or carbonates, are deposited in calcified structures from low concentrations in blood plasma and that the failure of glycerol solutions of potassium hydroxide (70) to extract the alkali metals is not comprehensible unless they are integral components of the inorganic structure. The comparative ease with which part of the carbon dioxide may be removed from bone by heat (12) does not prove the presence of free carbonates, since it has been shown that synthetic apatites containing carbonate lose perceptible amounts of carbon dioxide at comparatively low temperatures.

Klement has recently concluded that magnesium may replace calcium isomorphously in bone apatite (115).

C. Crystal orientation

According to a number of x-ray studies, the crystallites in enamel are preferentially orientated (6, 41, 43, 169, 188, 212, 213, 214), while those in dentine have a random arrangement (6, 41, 43, 212). Clark (43) reports that specimens of bone and enamel which he has examined have apatite crystals orientated in fibers. Thewlis (214) states that the orientation on the surface of enamel is different from the orientation in enamel sections.

There has been little effort, as yet, to determine the significance of crystallite orientation, except that Reynolds *et al.* (169) believe that one of the effects of fluorine in mottled teeth is to inhibit orientation and that this is one of the factors causing brittleness in fluoride teeth.

D. Physicochemical considerations

From time to time, efforts have been made to apply the methods of physical chemistry and the latest concepts of heterogeneous equilibria to the study of the mechanism of bone deposition. But these researches have, in the main, contributed little of value, because some of the restrictions imposed on thermodynamic methods have been violated. For example, the concept of solubility product is meaningless without reference to a known solid phase of comparatively simple ionic composition. Yet it has been stated (154) that "The generally accepted view is that calcification takes place in calcifying tissues from solutions rendered saturated or supersaturated when the product ($Ca^{++} \times PO_4^{---}$) exceeds the solubility product. The material deposited, 'the bone salt,' is an insoluble phosphate of the apatite series $3Ca_3(PO_4)_2 \cdot CaX_2$." Perhaps this is an exaggerated statement, but it is indicative of a tendency to use a concept without proper regard for its limitations (129, 130, 196).

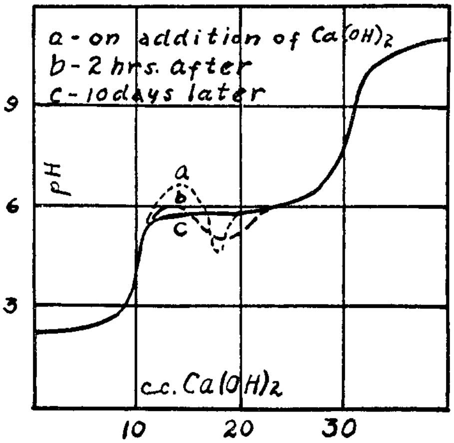

FIG. 10

Holt and his associates did attempt to identify the solid phase (82) before calculating solubility products (83, 84). They titrated phosphoric acid with limewater and confirmed the results of Wendt and Clarke (224), which are reproduced in figure 10.[32] They believed that the coincidence of the upper inflection point with the addition of exactly enough calcium hydroxide to form the tertiary compound indicated the existence of tricalcium phosphate. This compound, however, is almost certainly not capable of stable existence in aqueous solutions, especially at the pH of blood serum or the pH of the inflection point (12).

That smooth titration curves could be obtained in 8 to 10 days is further confirmation of the point made earlier that dicalcium phosphate reacts comparatively rapidly with solutions from which it precipitates.

[32] Britton (27) obtained similar results, but those of Hoffman and Gortner (79) were somewhat different.

But once it has been completely converted to a more basic form, the speed of reaction between solid and solution becomes very small. Thus, it is probable that the upper inflection point is due merely to rapid readjustment of ionic equilibria only slightly complicated by slow reactions with the solid phase.

Kramer, Shear, and associates have shown time and again, *in vivo* and *in vitro*, that the product Ca × P in solution is a criterion for calcification at the pH of serum (86, 121, 123, 201, 202, 203). Furthermore, in equilibration experiments with dicalcium phosphate at various pH values (202), the product, $[Ca^{++}] \times [HPO_4^{--}]$, calculated from theoretical considerations previously developed by others (72, 82, 83, 84, 196, 197), was found to be substantially constant. They suggested the interesting theory that dicalcium phosphate is the first substance precipitated in calcification and that the final basic compounds are obtained by subsequent hydrolysis (109, 201). Klement (111, 117) has recently supported this theory. However, there is no evidence of any kind that this compound occurs in bone. As a matter of fact, when Kramer *et al.* (121) investigated the composition of primary calcification (in which dicalcium phosphate, pure or partially hydrolyzed, should be found if it is to be found anywhere), they discovered that instead of the ratio of calcium to phosphorus being less than normal, it was considerably more.

Considering the complexity of the solid phase and the solution from which it precipitated, it seems hopeless to undertake research based on the assumption that "... initiation of precipitation of the bone salt depends alone on the concentrations of calcium, phosphate, and hydrogen ions" (130). The following statement by Murray (154) presents a more promising approach to the problem: "The fact that big differences in mineral content can occur in material deposited in different regions of the body at the same time promotes the suggestion that all calcifications are the result of specific cell activity rather than merely precipitation governed by solubility products."

Conclusion

According to Walden and Cohen (222), the criteria for the formation of solid solutions in ionic crystals which have been usually applied[33] "... may perhaps be valid for the occurrence of complete miscibility, but their force is certainly weak in the case of limited solubility." This observation seems to be supported by the apatite family, which furnishes an example of an ionic crystal capable of dissolving a large variety of

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[33] Identical types of chemical structure, identical types of crystal structure, and nearly identical lattice parameters.

components, in large or small proportions, without fundamental change in lattice.

Furthermore, it is contended that, at least for hydroxyapatite, a substance with some small whole number ratio of atomic species does not exist but rather a crystal lattice common to a continuous series of solid solutions.

The present uncertainties in our knowledge call for a new phase rule investigation of the basic region of the system CaO–P_2O_5–H_2O. Lengthy periods of contact between solid and solution should not be the sole method for obtaining equilibrium conditions. The method of Pearce and his associates (163, 164) may be adapted to this purpose, or precipitations may be carried out in concentrated solutions of inert salts in the hope that increased solubility will speed up the rate of reaction. Ammonium acetate is suggested, since it may easily be eliminated before analysis of the liquid phase. Carrying out reactions at high temperatures in bombs is another possibility.

But whatever method is used, time invariance of composition ought not to be the sole criterion of equilibrium. Equilibrium should be approached from opposite directions. This is possible, since it has been shown that compositions may be prepared which are either richer in CaO or richer in P_2O_5 than equilibrium compositions merely by altering the mode of precipitation.

Now that increased precision in x-ray methods is available (45, 46, 47, 222), a number of possibilities suggest themselves. The range of existence of solid solutions in the ternary system or in more complex apatite systems may be ascertained. The rôle played by the various constituents of bone and teeth may be established by determining the effect of changing composition on the lattice dimensions of the fundamental mineral matter.

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