

Empirical Border Lines of the Apatite Stability Field in the System $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}-\text{Na}_2\text{O}-\text{CO}_2-\text{MX}$ at Room Temperature

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Z. Naturforsch. **34c**, 165–170 (1979); received December 27, 1978

Calcium Phosphate, Apatite Solubility, Sodium Incorporation, Carbonate Incorporation

Literature data on equilibria between solid calcium phosphates having the apatite structure and aqueous solutions containing Na^+ and CO_3^{2-} ions were reexamined in view of the present data about the complexation of ions in such systems. Recalculations showed that all solutions were undersaturated or just saturated with respect to either brushite or octocalciumphosphate or more or less finely dispersed calcite and supersaturated with respect to pure hydroxylapatite. Sections through the quasi-sextary phase diagram were constructed which are representative for the system under simulated *in vivo* conditions.

Introduction

X-ray studies have established beyond question the apatitic nature of the main calcium phosphate phase in the mineral of bones and teeth [1], although other calcium phosphate phases can occur as well. It is also beyond doubt that sodium and carbonate are incorporated in the apatite phase and that this causes the adaptability of the apatite phase to a hugh range of apparent solubility products in such a way that Na^+ and CO_3^{2-} incorporation leads to increased solubility. It seems further that in mammals and man many body fluids are close to equilibrium with the apatite of their bones [2] whereby the relative differences of the Na^+ and CO_3^{2-} content of these body fluids can in principle explain the apparent differences in composition of the bone mineral between species and within each bone of one species. Qualitatively, it is expected that incorporation of more Na^+ and CO_3^{2-} ions in the apatite phase will lead to a further increase of its solubility. It is not clear what significance this might have for the rate of the energy conversion through the phosphate metabolism in the organism and for all the biochemical cycles that depend on it. At the moment it is possible only to estimate the limits of the apatite stability field as they apply to the living organism. The purpose of this paper is to make such an estimate on the basis of published experimental data for equilibrations of calcium phosphates in Na^+ and CO_3^{2-} con-

taining aqueous solutions. Possible exchange reactions controlling the equilibrium between an apatite phase and such aqueous solutions have been discussed in more detail elsewhere [3] although their significance has been recognized a long time ago [1].

Equilibria in the System $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}-\text{MX}$

Precipitation studies in the acidic range ($\text{pH} \leq 6$) of the system $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}$ have shown that the solid formed first from an aqueous solution containing calcium and phosphate ions is most probably brushite (DCPD or $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$). In the range $\text{pH} \geq 7$ octocalciumphosphate (OCP or $\text{Ca}_8(\text{HPO}_4)_2(\text{PO}_4)_4 \cdot 5\text{H}_2\text{O}$) is formed initially. Both phases transform into hydroxylapatite (OHA or $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) upon hydrolysis in the range $\text{pH} \geq 4.5$. Below $\text{pH} 4$ brushite is stable. Good values for the solubility products of brushite, octocalciumphosphate and hydroxylapatite are 2.6×10^{-7} , 2×10^{-69} and 3×10^{-118} respectively [4]. Elsewhere representations of the underlying phase diagram were given as a plot of the total calcium concentration versus the pH [2] or as a plot of calcium *versus* phosphate concentration [4].

Extension has been made of the ternary system $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}$ into a quasi-quaternary system by defining a quantity U (\pm) when there is either an excess of acid HX or an excess of base MOH present in the system [4]. The acid or base must contain anions or cations respectively that do not interfere with the calcium phosphates in such a way that they alter their solubility products or form complexions with calcium or any of the phosphate ions in the aqueous solution. Representations of this quasi-

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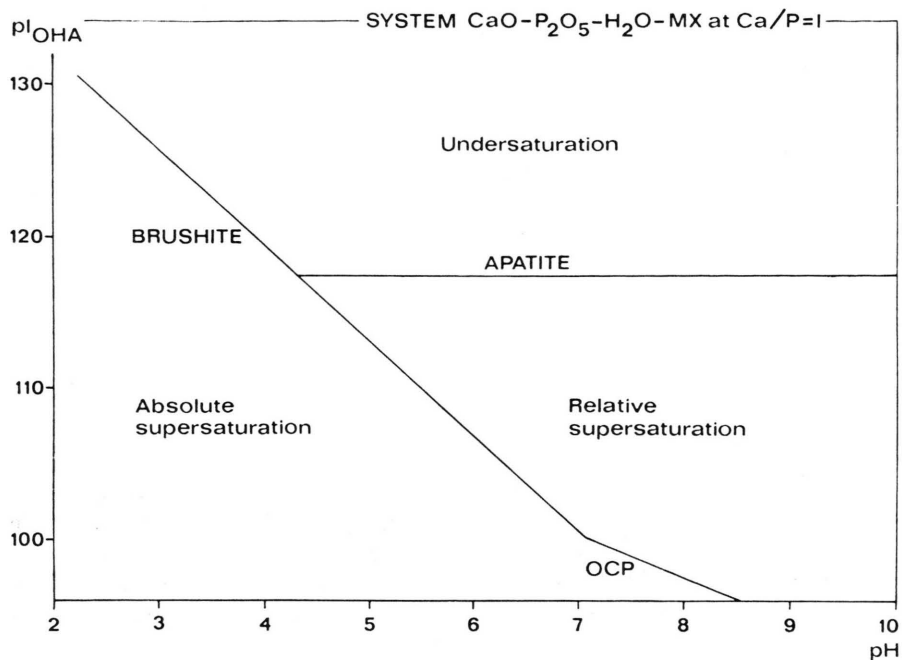


Fig. 1. Solubility isotherms for the ternary compounds brushite $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$, hydroxylapatite $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ and octocalciumphosphate $\text{Ca}_8(\text{HPO}_4)_2(\text{PO}_4)_4 \cdot 5\text{H}_2\text{O}$ in the quaternary system $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}-\text{MX}$ at a molar ratio $\text{Ca}/\text{P}=1$ in the aqueous phase. Hereby $p\text{I}_{\text{OHA}} = 10 p\text{Ca} + 6 p\text{PO}_4 + 2 p\text{OH}$.

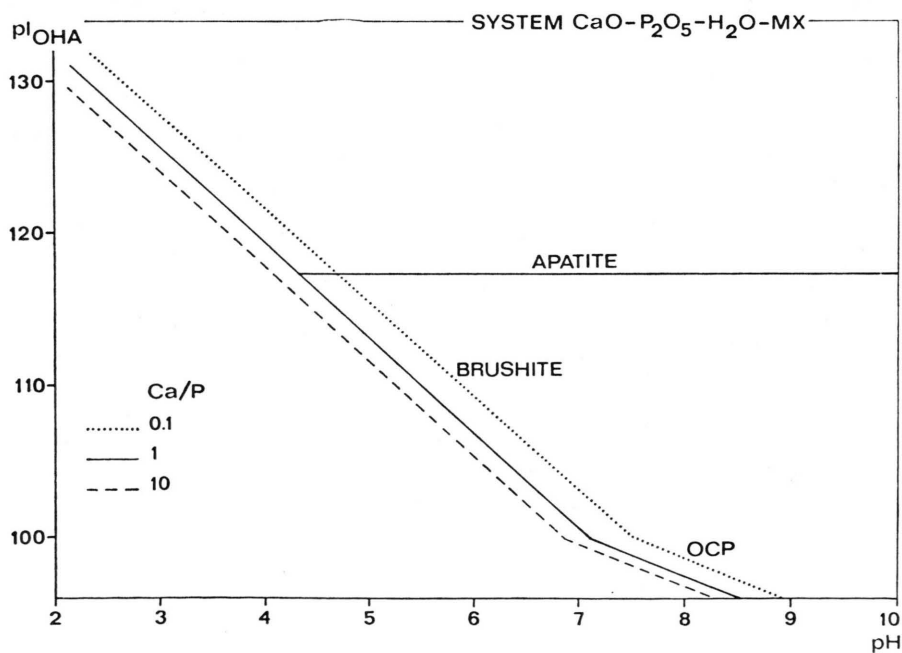


Fig. 2. Solubility isotherms for the ternary compounds brushite, hydroxylapatite and octocalciumphosphate in the quaternary system $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}-\text{MX}$ at different Ca/P ratio's in the aqueous phase.

quaternary system $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}-\text{MX}$ are given in this study as a plot of the negative logarithm of the ionic product for hydroxylapatite pI_{OHA} versus pH. In Fig. 1 the regions of undersaturation, relative supersaturation and absolute supersaturation at a molar Ca/P ratio of 1 are designated and they appear to be separated by straight lines. These plots are analogues to those of Pourbaix *et al.* [5]. As follows from Fig. 2, the position of the borderlines for brushite and octocalciumphosphate formation depends slightly on the Ca/P ratio in the aqueous phase. In these diagrams the field of relative supersaturation with respect to OCP and simultaneous undersaturation with respect to brushite has not been indicated, although it plays a role in the description of kinetic phenomenon occurring between calcium phosphates, e.g. brushite can be transformed into octocalciumphosphate by careful hydrolysis at a $\text{pH} \geq 6.3$ [6].

Equilibria in the System

$\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}-\text{Na}_2\text{O}-\text{CO}_2-\text{MX}$

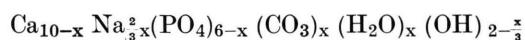
Many authors have investigated equilibria in this system with the purpose to simulate the *in vivo* system where Na^+ and CO_3^{2-} ions are abundant. Unfortunately, only a few data contain all the information relevant to such equilibria [3], *i. e.* pH and the total content of calcium, phosphate, sodium and carbonate of the equilibrated aqueous solutions. They are compiled in Table I. Two other criteria were applied in the selection of these data. Firstly no solid phase other than apatite should have been used to constitute the system. Secondly, other electrolytes interfering with the calcium phosphates by

altering their relative stability (Mg^{2+}), as well as biopolymers and other complexing agents (citrate, lactate, etc.) should have been absent.

For these data the negative logarithm of the ionic products for hydroxylapatite, brushite, octocalciumphosphate and calcite (CaCO_3) were calculated using the following constants: for H_2CO_3 $\text{pK}_1 = 6.37$ and $\text{pK}_2 = 10.25$, for H_3PO_4 $\text{pK}_1 = 2.12$, $\text{pK}_2 = 7.21$ and $\text{pK}_3 = 12.67$ and for the complexes NaCO_3^- , NaHCO_3 , CaHCO_3^+ , CaCO_3^0 , NaHPO_4^- , $\text{CaH}_2\text{PO}_4^+$, CaHPO_4^0 and CaPO_4^- the pK for dissociation being $+1.27$, -0.25 , $+1.26$, $+3.2$, $+1.15$, $+0.73$, $+2.41$ and $+6.46$ [15–17]. It must be noticed that in all investigations mentioned in Table I, the pH and the total concentrations of calcium and phosphate were determined after equilibration, whereas those of sodium and carbonate were either determined after equilibration or, for the sake of the calculations, they were assumed to be approximately equal to the initial concentrations.

The calculations showed that none of the equilibrated solutions was saturated or supersaturated with respect to brushite or octocalciumphosphate, whereas about 80% of the solutions were undersaturated or saturated with respect to calcite ($\text{pK}_{\text{CaCO}_3} = 8.34$) and the others seemed to be supersaturated with respect to calcite (see discussion). However, all solutions were supersaturated with respect to pure hydroxylapatite.

For reasons mentioned in the introduction it is assumed that not pure hydroxylapatite but Na^+ and CO_3^{2-} -containing apatites have been the relevant solid phase in these experiments. It is further assumed that the Na^+ and CO_3^{2-} -containing apatites can be represented by a formula like that published by Bonel, Labarthe and Vignoles [26]



so that hydroxylapatite is thought to be the end member of a continuous series of solid solutions with the apatite structure. Analogously to exchanges of OH^- by F^- ions [27] the surface of such apatite crystals can exchange ions with the aqueous phase and, as a consequence, the crystals show a solubility behaviour in accordance with the composition x of their surface layer after equilibration. It is hypothesized here that the above mentioned supersaturation with respect to pure hydroxylapatite is to be interpreted as the fact that the relevant aqueous solutions

Table I. Compilation of literature data for equilibrations in the system $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}-\text{Na}_2\text{O}-\text{CO}_2-\text{MX}$.

Reference	Remarks	Number of equilibrations
Kuyper, 1945	Table 1	10
Holt, LaMer and Chown, 1925	Table 9	11
Sendroy and Hastings, 1927	Table 2	5
Bachra, Trautz, and Simon, 1965	Fig. 2 c	30
Grøn, Spinelli, Trautz, and Brudevold, 1963	Table 1	6
Greenwald, 1945	Table 2	10
Logan and Taylor, 1937	Tables 1 and 2	13
Kleinmann, 1928	Tables 10, 11 and 19	10

have been in equilibrium with an apatite surface layer containing some Na^+ and CO_3^{2-} ions. Thereby, it is to be expected that an increase in the solubility is related to an increased Na^+ and CO_3^{2-} content of the surface layer of the apatite particles. A more precise model and a more quantitative interpretation of the data of Table I sustaining this hypothesis will be given elsewhere [18]. Thus the apparent supersaturation of many body fluids with respect to pure hydroxylapatite is interpreted as a state of saturation or slight undersaturation with respect to the Na^+ and CO_3^{2-} -containing apatite relevant to the inorganic composition of those body fluids.

The consequence of this Na^+ and CO_3^{2-} -incorporation into the apatite for the form of the phase diagram of the quasi-sextary system $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}-\text{Na}_2\text{O}-\text{CO}_2-\text{MX}$ is then as presented in Fig 3 and Fig. 4: the line for apatite stability of Figs 1 and 2 is transformed into an apatite stability field. The positions of the border lines for brushite or octocalciumphosphate depend on the Ca/P ratio in the aqueous phase, that for calcite depends on both Ca/P and P_{CO_2} . In this context it may be mentioned that $P_{\text{CO}_2} = 5.3 \text{ kPa}$ equals the value for the internal medium in the human body (40 mm Hg). It must be realised that each point of the apa-

tite stability fields of these figures can be realised in keeping with two degrees of freedom according to the phase rule, so that Figs 3 and 4 must be considered as projections of sections through the multi-dimensional phase diagram, as they are used frequently in this type of representations [15].

Discussion

In the experiments where supersaturation with respect to calcite was apparent a finely dispersed calcite phase might have been present. Taking into account an effective surface energy of about 0.1 J m^{-2} or 100 erg/cm^2 [19] and a critical nucleus size of 1.2 nm, one calculates a maximum solubility product of 5×10^{-8} ($\text{pK} = 7.30$). As $\text{pI}_{\text{CaCO}_3}$ for all data was higher than this pK value, it can be concluded that the theoretical border line for calcite formation as depicted in Figs 3 and 4 describes the equilibria in the quasi-sextary system, if calcite is taken into consideration in a more or less finely dispersed form.

As far as the apatite phase is concerned, reported values for the effective surface energy are in the range $0.1 - 0.4 \text{ J m}^{-2}$ or $100 - 400 \text{ erg/cm}^2$ whereas an average crystal size of 30 nm is typical for preparations by precipitation from aqueous solutions

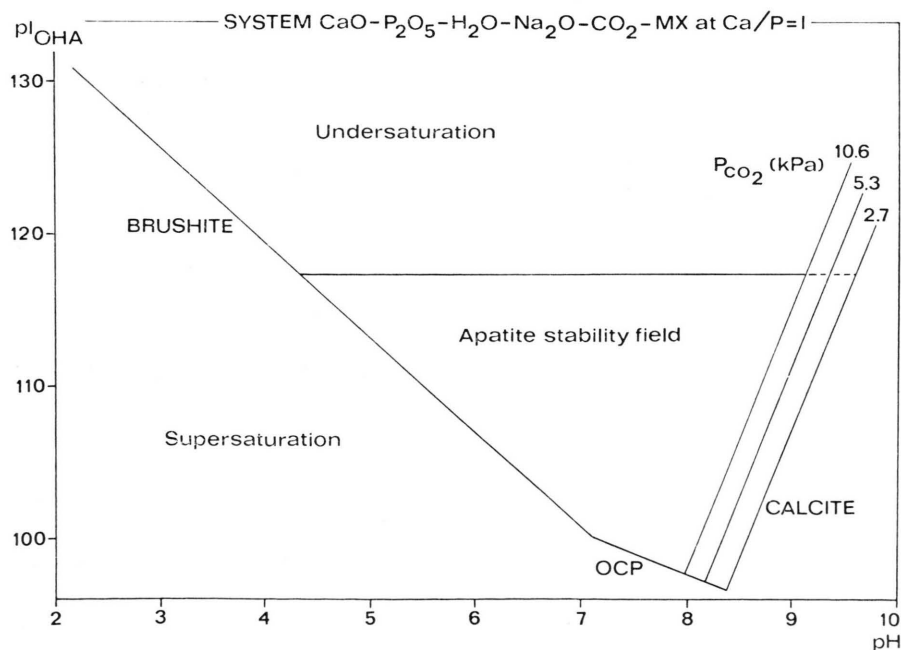


Fig. 3. Empirical borderlines of the apatite stability field in the quasi-sextary system $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}-\text{Na}_2\text{O}-\text{CO}_2-\text{MX}$ at $\text{Ca/P}=1$ and under different carbon dioxide partial pressures.

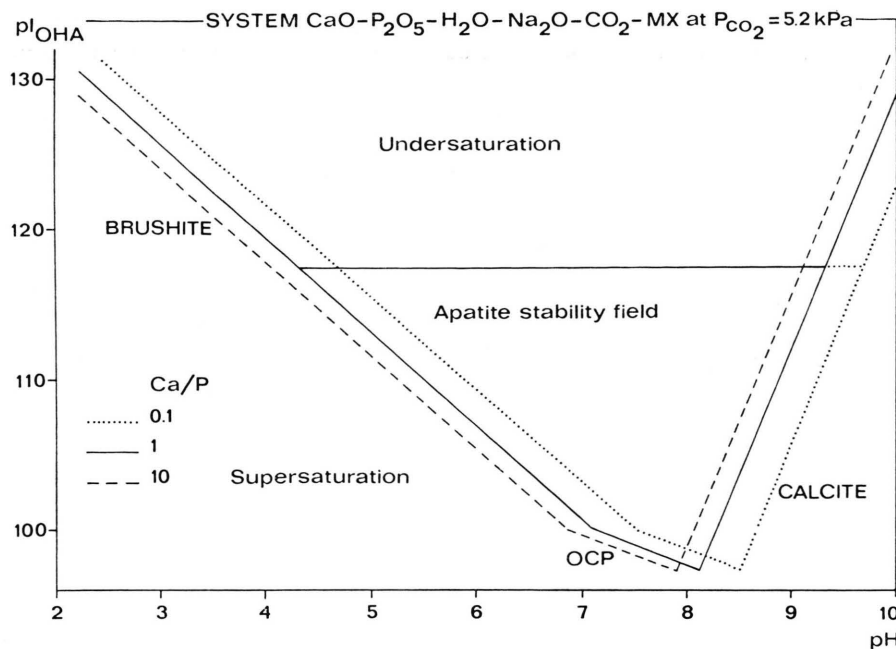


Fig. 4. Empirical borderlines of the apatite stability field in the quasi-sextary system $\text{CaO}-\text{P}_2\text{O}_5-\text{H}_2\text{O}-\text{Na}_2\text{O}-\text{CO}_2-\text{MX}$ at different Ca/P ratio's under a carbon dioxide partial pressure of 5.2 kPa (40 mm Hg).

[20]. This allows for a decrease of up to 1 unit in the pK value for hydroxylapatite. The pI_{OHA} values derived from the experimental data exceed this decrease by up to 20 units in the majority of the equilibria. Therefore, the incorporation of Na^+ and CO_3^{2-} ions in the apatite structure remains most probably as the primary cause of the decrease in pI_{OHA} apparent from our calculations although the particle size might have contributed to the effective decrease of the pI_{OHA} in those data where the solid phase was formed by precipitation, making up about 55% of the data. In the other and also in the experiments by Ericsson [21] apatite was present as a well defined phase from the beginning of equilibration so that neither the effect of particle size nor that of ion entrapment are acceptable explanations for the observed behaviour of these apatitic systems. The incorporation of Na^+ and CO_3^{2-} ions remains as the most serious possibility for causing the increased solubility in Na^+ and CO_3^{2-} containing mediums.

As far as the accuracy of representations such as given in Fig. 1 through 4 is concerned, they depend on the standard deviation of the solubility products of the compounds brushite, octocalciumphosphate and calcite and also on the fact whether these are affected by the presence of Na^+ and CO_3^{2-} ions at all.

The solubility product for brushite [16] at 25 °C equals $2.57 (\pm 0.01) \cdot 10^{-7}$, that for octocalciumphosphate [22, 6] is about 2×10^{-69} and may contain an error of 50%, whereas that of calcite [23] is $3.3 (\pm 0.7) \cdot 10^{-9}$. According to Olsen, Watanabe and Cole [24], Na^+ and CO_3^{2-} ions do not have an appreciable effect on the solubility product of brushite, whereas O'Connor and Cadena [23] have shown that the solubility product of calcite is independent of the Na^+ concentration. It is not known whether the solubility product of octocalciumphosphate depends on the presence of Na^+ and CO_3^{2-} ions.

As far as the validity of representations such as given in Fig. 1 through 4 is concerned, real systems in ecology, biology and medicine may also contain other (trace) ions such as Mg^{2+} , Fe^{2+} , Zn^{2+} , F^- . It is known that the F^- ion affects the stability of the apatite phase. If traces of Fe^{2+} or other divalent transition metal ions would not be present, monetite CaHPO_4 rather than brushite $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ might form in the low pH range [25]. This would shift the according borderline somewhat to higher pH values as monetite is slightly more stable than brushite [4]. The presence of Mg^{2+} ions would lead to the formation of a whitlockite phase [26]. This Mg-containing calcium phosphate is isomorphous with β -tertiary calcium phosphate which can be formed

at high temperatures, and which develops a solubility intermediary between that of hydroxylapatite and octocalciumphosphate [4]. A thorough examination of these effects of other trace elements is necessary

in order to find a physico-chemical basis relevant to the behaviour of real calcium phosphate systems containing these additional ions.

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