Empirical Border Lines of the Apatite Stability Field in the System 
CaO—P₂O₅—H₂O—Na₂O—CO₂—MX at Room Temperature

F. C. M. Driessens, J. W. E. van Dijk *, and J. M. P. M. Borggreven
Institute for Dental Materials and Laboratory for Oral Biochemistry, Subfaculty of Dentistry, University of Nijmegen, P. O. Box 9101, 6500 HB Nijmegen, The Netherlands

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Literature data on equilibria between solid calcium phosphates having the apatite structure and aqueous solutions containing Na⁺ and CO₃²⁻ 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 hydroxyapatite. 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 adaptibility of the apatite phase to a high range of apparent solubility products in such a way that Na⁺ and CO₃²⁻ 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 whereby the relative differences of the Na⁺ and CO₃²⁻ 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 CO₃²⁻ 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 equilibria of calcium phosphates in Na⁺ and CO₃²⁻ containing 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 CaO—P₂O₅—H₂O—MX

Precipitation studies in the acidic range (pH ≤ 6) of the system CaO—P₂O₅—H₂O have shown that the solid formed first from an aqueous solution containing calcium and phosphate ions is most probably brushite (DCPD or CaHPO₄·2H₂O). In the range pH ≥ 7 octocalciumphosphate (OCP or Ca₈(PO₄)₆(OH)₂) is formed initially. Both phases transform into hydroxyapatite (OHA or Ca₁₀(PO₄)₆(OH)₂) upon hydrolysis in the range pH ≥ 4.5. Below pH 4 brushite is stable. Good values for the solubility products of brushite, octocalciumphosphate and hydroxyapatite are 2.6 × 10⁻²⁸, 2 × 10⁻⁶⁹ and 3 × 10⁻¹⁴⁸ 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 CaO-P₂O₅—H₂O into a quasi-quaternary system by defining a quantity U (±) 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 complexes with calcium or any of the phosphate ions in the aqueous solution. Representations of this quasi-
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 quasiquaternary system $\text{CaO} - \text{P}_2\text{O}_5 - \text{H}_2\text{O} - \text{MX}$ at a molar ratio Ca/P = 1 in the aqueous phase. Hereby $\text{pI}_{\text{OHA}} = 10 \text{pCa} + 6 \text{pPO}_4 + 2 \text{pOH}$.

Fig. 2. Solubility isotherms for the ternary compounds brushite, hydroxylapatite and octocalciumphosphate in the quasiquaternary 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 $\text{CaO} - \text{P}_2\text{O}_5 - \text{H}_2\text{O} - \text{Na}_2\text{O} - \text{CO}_2 - \text{MX}$ are given in this study as a plot of the negative logarithm of the ionic product for hydroxyapatite $p_{\text{IOHA}}$ 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 or octocalciumphosphate, e.g. brushite can be transformed into octocalciumphosphate by careful hydrolysis at a 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 hydroxyapatite, brushite, octocalciumphosphate and calcite ($\text{CaCO}_3$) were calculated using the following constants: for $\text{H}_2\text{CO}_3$ $pK_1 = 6.37$ and $pK_2 = 10.25$, for $\text{H}_2\text{PO}_4$ $pK_1 = 2.12$, $pK_2 = 7.21$ and $pK_3 = 12.67$ and for the complexes $\text{NaCO}_3^-$, $\text{NaHCO}_3^-$, $\text{CaHCO}_3^+$, $\text{CaCO}_3^{6+}$, $\text{NaHPO}_4^-$, $\text{CaH}_2\text{PO}_4^+$, $\text{CaHPO}_4^{6-}$ and $\text{CaPO}_4^{-}$ the $pK$ for dissociation being $+1.27$, $-0.25$, $+1.12$, $+3.2$, $+1.15$, $+0.73$, $+2.41$ 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 ($pK_{\text{CaCO}_3} = 8.34$) and the others seemed to be supersaturated with respect to calcite (see discussion). However, all solutions were supersaturated with respect to pure hydroxyapatite.

For reasons mentioned in the introduction it is assumed that not pure hydroxyapatite 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]

$$\text{Ca}_{10-x}\text{Na}_{x}^{3+}(\text{PO}_4)_6-x(\text{CO}_3)_x(\text{H}_2\text{O})_x(\text{OH})_{2-x}$$

so that hydroxyapatite 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 hydroxyapatite is to be interpreted as the fact that the relevant aqueous solutions...
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 hydroxyapatite 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 CaO—P\(_2\)O\(_5\)—H\(_2\)O—Na\(_2\)O—CO\(_2\)—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\(_{CO_2}\) = 5.3 kPa equals the value for the internal medium in the human body (40 mm Hg). It must be realised that each point of the apatite 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 multidimensional 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 \(\times\) 10\(^{-8}\) (pK = 7.30). As pI\(_{CaCO_3}\) 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 J m\(^{-2}\) or 100 — 400 erg cm\(^{-2}\) whereas an average crystal size of 30 nm is typical for preparations by precipitation from aqueous solutions.

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![Fig. 3. Empirical borderlines of the apatite stability field in the quasi-sextary system CaO—P\(_2\)O\(_5\)—H\(_2\)O—Na\(_2\)O—CO\(_2\)—MX at Ca/P=1 under different carbon dioxyde partial pressures.](image-url)
Fig. 4. Empirical borderlines of the apatite stability field in the quasi-sextary system CaO—P₂O₅—H₂O—Na₂O—CO₂—MX at different Ca/P ratios 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 pIoha 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 CO₃²⁻ ions in the apatite structure remains most probably as the primary cause of the decrease in pIoha apparent from our calculations although the particle size might have contributed to the effective decrease of the pIoha 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 apatic systems. The incorporation of Na⁺ and CO₃²⁻ ions remains as the most serious possibility for causing the increased solubility in Na⁺ and CO₃²⁻ containing mediums.

As far as the accuracy 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 Mg²⁺, Fe²⁺, Zn²⁺, F⁻. It is known that the F⁻ ion affects the stability of the apatite phase. If traces of Fe²⁺ or other divalent transition metal ions would not be present, monetite CaHPO₄ rather than brushite CaHPO₄·2H₂O 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 Mg²⁺ 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 octocalcium phosphate [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.