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Calcium Phosphate Crystallization. IV. Kinetics of Heterogeneous Nucleation of Tetracalcium Monohydrogen Phosphate on Brushite Crystals

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The kinetics of heterogeneous nucleation of OCP ($Ca_4H(PO_4)_3 \cdot 2.5H_2O$) on brushite ($CaHPO_4 \cdot 2H_2O$) at 37 °C has been studied, partly by pH-static titration with calcium hydroxide. Nucleation is strongly favoured by crystal defects of the substrate. At constant supersaturation the rate of crystallization of OCP is initially very low, thereafter being in accordance with the rate expression $M(t) = k(t - t_i)^4$, where $M(t)$ is the amount of OCP formed at time t, and t_i is the induction time. The stationary nucleation rate calculated from k follows the classical (Becker-Döring-Volmer) expression, but the critical nucleus contains only 1–2 formula units. t_i increases in steps with decreasing supersaturation. This is most easily understood if it is assumed that t_i is not the induction time for nucleation, but rather a relaxation time of the critical nucleus.

In a previous paper[1] we reported the pH-static titration of a mixed suspension of brushite ($CaHPO_4 \cdot 2H_2O$) and OCP ($Ca_4H(PO_4)_3 \cdot 2.5H_2O$) with calcium hydroxide as a useful means of determining the overall growth kinetics of OCP. The essential points were that (1) the rate of dissolution of brushite is so high that the solution is always saturated with respect to the latter, and (2) calcium hydroxide is one of the components of the system. The consequence of these two facts is that the whole process takes place at constant supersaturation. Clearly, the method should also be useful in studying the heterogeneous nucleation of OCP on brushite. The present paper reports the results of such a study.

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EXPERIMENTAL

The pH-static titrations were carried out as previously described[1] with the exception that 0.5 g of brushite and no OCP was added to the dilute phosphoric acid solution. In addition, some experiments were carried out in which pH was allowed to vary freely, following the procedure described in the first paper in this series.[2]

The brushite used for all the experiments was separated into a number of fractions according to crystal size, using sieves with 90, 105, 125, 149, 180 and 250 μm mesh size.

All experiments were carried out at 37 °C. This temperature was chosen for its physiological importance and because it yielded a suitable reaction rate.

RESULTS

Fig. 1 shows an example of unusually well-developed OCP spherulites on a brushite crystal. It is evident that OCP is indeed formed by heterogeneous nucleation. Preliminary experiments with freely varying pH were carried out to determine the effect of crystal size on the induction time t_i. It was found that t_i decreased with increasing crystal size for constant total mass of brushite; Fig. 2 shows some of the results. A sample of crystals < 90 μm which had been compressed in a steel cylinder to about 60 MPa for a couple of seconds showed a significantly reduced induction time (Fig. 2).

All pH- static titrations were carried out with the 149–180 μm fraction. A series of experiments with the 90–105 μm fraction was abandoned after a few

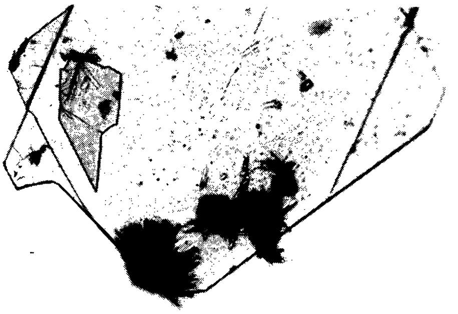

Fig. 1. Brushite crystal with OCP spherulites. The brushite crystal is about 0.5 mm across.

trials, because crystallization of OCP took place on all surfaces in the cell, not only on the brushite crystals. With the former fraction, a typical plot of the amount of OCP formed (equal to the amount of $Ca(OH)_2$ consumed) *versus* time had the appearance as shown in Fig. 3. Experiments were carried out at mean pH intervals of 0.05 units. The comments in Ref. 1 concerning the limits of precision apply to the present study as well.

DISCUSSION

From the form of Fig. 2 it is concluded that nucleation of OCP is strongly favoured by crystal defects, which are more abundant in large than in small crystals. If nucleation were equally probable all over the surface, we should expect the induction time to increase with increasing crystal size (equivalent with decreasing specific surface), contrary to our observation.

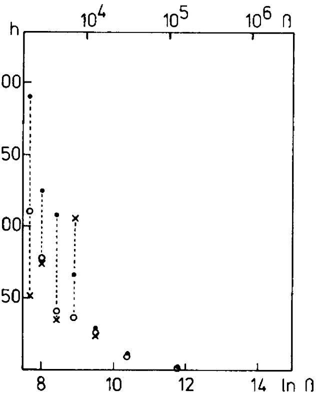

Fig. 2. Induction time by variable pH as a function of initial supersaturation. Crystal size of brushite 180 − 250 μm. ○; crystal size of brushite <90 μm, ●; same after compression to 60 MPa, ×.

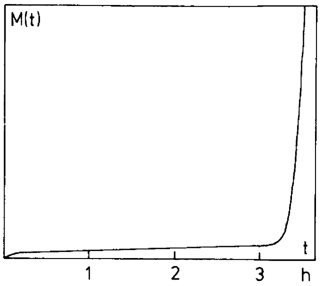

Fig. 3. Amount of OCP formed (in arbitrary units) as a function of time for ln $\beta = 8.27$.

Curves similar to Fig. 3 have been observed by Dugua and Simon[3,4] for the crystallization of sodium perborate at constant supersaturation. As shown by Gindt and Kern[5] the total mass $M(t)$ crystallized at time t is given by the convolution integral (1), where $J(t_0)$ is the nucleation frequency at

$$M(t) = \int_0^t J(t_0) m(t-t_0) \mathrm{d}t_0 \qquad (1)$$

time t_0 and $m(t-t_0)$ is the mass of a single crystal formed at time t_0. Eqn. (1) is valid only for constant supersaturation, and it is assumed that the evolution of a single crystal is independent of t_0. If the individual crystal faces advance with constant linear velocity, we have eqn. (2), where A is a function of

$$m(t-t_0) = A(t-t_0)^3 \qquad (2)$$

supersaturation. If J were constant, we should simply have eqn. (3). As Fig. 4 shows, $M(t)^{1/4}$ is partly

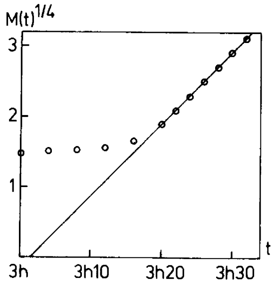

Fig. 4. Fourth root of the ordinate in Fig. 2 as a function of time.

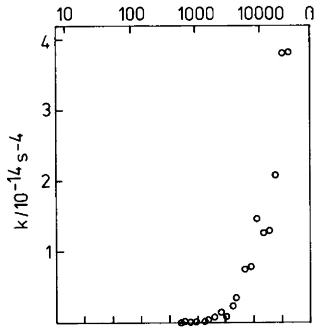

Fig. 5. k from eqn. (4) as a function of supersaturation.

$$M(t) = \tfrac{1}{4} J A t^4 \tag{3}$$

a linear function of t, but the part of the curve for which this is valid is given by eqn. (4). For $t < t_i$ the

$$M(t) = k(t - t_i)^4 \tag{4}$$

rate of crystallization is very low and difficult to analyze.

Taking the fourth derivative of $M(t)$ according to eqn. (1) and (2) yields eqn. (5) and similarly, from eqn.

$$M^{(4)}(t) = 6AJ(t) \tag{5}$$

$$M^{(4)}(t) = 6k \tag{6}$$

(4), eqn. (6), whence $k = AJ_s$, where J_s is the steady-state rate of nucleation. The shape of our curves shows that $J(t)$ is very low initially and then, in a rather short time interval around t_i, increases to the limiting value J_s. This means that the frequently quoted expression,[5] eqn. (7), does not apply to the present case.

$$J(t) = J_s \exp(-t_i/t) \tag{7}$$

Fig. 5 shows k as a function of $\ln \beta$, where β is the ratio between the ionic product and the solubility product of OCP. A in eqn. (2) is proportional to R^3, where R is the average rate of growth of a crystal face on OCP, known as a function of β from our previous investigation.[1] According to eqn. (5) and (6) $k/R^3 = k'$ is proportional to the steady-state nucleation rate J_s.

The heteronuclei are either two-dimensional, cap-shaped (rounded), or polyhedral, like an ordinary crystal. As OCP crystallizes in spherulites, the latter case is not very likely, because such a nucleus would be expected to develop into a single crystal. The Gibbs function of formation of a two-dimensional heteronucleus containing N formula units is given by eqn. (8), where $\bar{s}$ is the surface area of one formula

$$\Delta G(N) = N[-kT \ln \beta + (\gamma_{nl} - \gamma_{sl} + \gamma_{ns})\bar{s}] + 4\lambda\sqrt{\bar{s}N} \tag{8}$$

unit in the nucleus, γ_{nl}, γ_{sl}, and γ_{ns} are the nucleus-liquid, substrate-liquid, and nucleus-substrate interfacial tensions, respectively, and λ is the edge free energy per unit length of the nucleus, assumed to be quadratic in shape. Eqn. (8) leads to the expression (9) for J_s,[6,7]

$$J_s = f\{c_i\} \exp\left(-\frac{4\lambda^2\bar{s}}{kT[kT\ln\beta - (\gamma_{nl} - \gamma_{sl} + \gamma_{ns})\bar{s}]}\right) \tag{9}$$

where $f\{c_i\}$ is a function of the concentrations of the different ionic species present. As the system is always in equilibrium with respect to brushite, the surface concentrations will not change much, whence we shall treat $f\{c_i\}$ as a constant. When $\gamma_{nl} - \gamma_{sl} + \gamma_{ns} > 0$, which corresponds to imperfect wetting in the case of a liquid drop on a solid surface, eqn. (9) predicts the existence of a critical supersaturation, eqn. (10), below which two-

$$\beta_{crit} = \exp\left(\frac{(\gamma_{nl} - \gamma_{sl} + \gamma_{ns})\bar{s}}{kT}\right) \tag{10}$$

dimensional nucleation can no longer take place (but the two other possibilities still exist). The slope of a plot of $\ln J_s$ against $1/\ln \beta$ should tend to $-4\lambda^2\bar{s}/k^2T^2$ for high β and to $-\infty$ as $\beta \rightarrow \beta_{crit}$.

If the nucleus is cap-shaped (we assume a spherical cap), we may introduce the contact angle α with the aid of Young's equation, eqn. (11).

$$\gamma_{sl} = \gamma_{ns} + \gamma_{nl} \cos \alpha \tag{11}$$

The area of the nucleus-liquid interface is then given by eqn. (12), whereas the area of the nucleus-

$$A_{nl} = 2\pi r^2 (1 - \cos \alpha) \tag{12}$$

substrate interface is as eqn. (13), where r is the radius of curvature of the cap. Instead of eqn. (8) we now find, using eqn. (11), eqn. (14).

$$A_{ns} = \pi r^2 \sin^2\alpha \tag{13}$$

$$\Delta G(N) = -NkT\ln\beta + \pi r^2\gamma_{nl}(1-\cos\alpha)(2-\cos\alpha-\cos^2\alpha) \tag{14}$$

The volume of the nucleus is given by eqn. (15), where $\bar{v}$ is the volume of one formula unit in the nucleus. We may now express ΔG as a function of r; eqn. (16)

$$V_n = \frac{\pi}{3}r^2(1-\cos\alpha)(2-\cos\alpha-\cos^2\alpha) = N\bar{v} \tag{15}$$

$$\Delta G(r) = \left(-\frac{\pi}{3}\frac{r^3}{\bar{v}}kT\ln\beta + \pi r^2\gamma_{nl}\right)(1-\cos\alpha)(2-\cos\alpha-\cos^2\alpha) \tag{16}$$

$$r^* = \frac{2\gamma_{nl}\bar{v}}{kT\ln\beta} \tag{17}$$

The radius of the critical nucleus is given, as usual, by the Gibbs-Kelvin equation, eqn. (17), and the nucleation rate will now be as eqn. (18), which, apart from geometrical factors, corresponds to the classical expression for three-dimensional nucleation.[6,7]

$$J_s = f\{c_i\}\exp\left[-\frac{4\pi}{3}\frac{\gamma_{nl}^3\bar{v}^2}{k^3T^3\ln^2\beta}(1-\cos\alpha)(2-\cos\alpha-\cos^2\alpha)\right] \tag{18}$$

As Figs. 6 and 7 show, both the two-dimensional and the spherical cap nucleus may explain the present data. From the slopes of the regression lines we find the following parameter values:

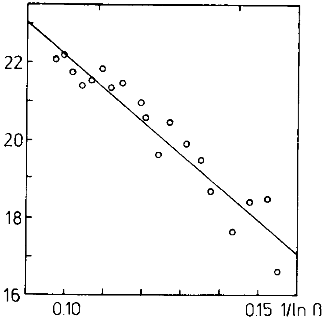

Fig. 6. Test of two-dimensional nucleation.

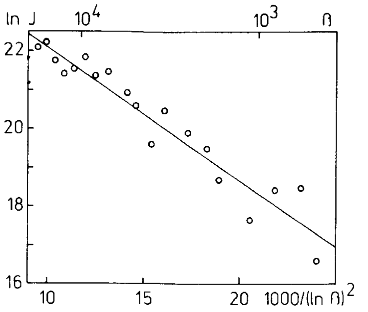

Fig. 7. Test of nucleation with cap-shaped nuclei.

$$\lambda\sqrt{\bar{s}} = 11.9 \text{ kJ/mol}$$

for the two-dimensional nucleus and

$$\gamma_{nl}\bar{v}^{2/3}[(1-\cos\alpha)(2-\cos^2\alpha)]^{1/3} = 11.2 \text{ kJ/mol}$$

for the spherical cap nucleus. The value of $\lambda\sqrt{\bar{s}}$ is not very far from that found for the surface-nucleation growth mechanism of OCP.[1] As we do not known α, we are unable to calculate γ_{nl}.

For $\beta \gg \beta_{crit}$, the number of formula units in the critical two-dimensional nucleus is given by eqn. (19).

$$N^* = \frac{4\lambda^2\bar{s}}{(kT\ln\beta)^2} \tag{19}$$

The corresponding value for the cap-shaped nucleus is found from eqns. (15) and (17); eqn. (20).

$$N^* = \frac{8\pi}{3}\frac{\gamma_{nl}^3\bar{v}^2}{(kT\ln\beta)^3}(1-\cos\alpha)(2-\cos\alpha-\cos^2\alpha) \tag{20}$$

In both cases we find that the critical nucleus contains from a little less than 1 to a little more than 2 formula units. The smallest electrically neutral nucleus is $Ca_3(PO_4)_2\cdot xH_2O$, and $N^*=2$ corresponds to the formula $Ca_8H_2(PO_4)_6\cdot 5H_2O$, *i.e.* it contains 19 particles. From this it is obvious that a distinction between the two shapes of a nucleus has no real significance. Furthermore, we should expect such a small nucleus to possess structural features not found in a macroscopic crystal,[8-10] which may explain why it develops into a spherulite instead of a single crystal.

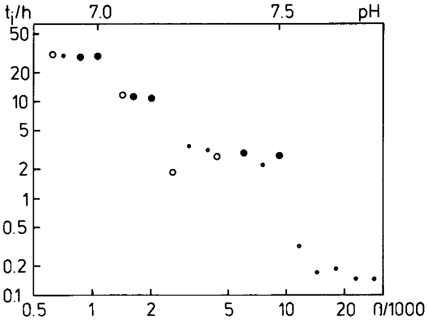

Fig. 8. Induction time as a function of supersaturation. Different symbols indicate results from different series of experiments.

The induction time t_i depends on β in a very peculiar way (Fig. 8). This is obviously a step function. The only possible explanation of this behaviour is that the size of the critical nucleus is not a continuous variable and that it solely determines the value of t_i, without any explicit influence from the composition of the surrounding solution. Thus is seems unlikely that t_i should be the induction time for nucleation in the usual sense; we believe it to represent some kind of relaxation time of the nucleus.

What probably takes place is the following: Critical clusters – not nuclei, because their structure is different from that of the OCP crystal – are formed on the furface of the brushite crystals with frequency J; their size is a step function of β, increasing with decreasing β. After the formation of a critical cluster, it undergoes a transformation, the nature of which we do not know at present. This transformation takes the time t_i, and then crystals start to grow in many different directions from the cluster. With this model, we have

$$m(t)=\begin{cases}0 \text{ for } t\le t_i \\ A(t-t_i)^3 \text{ for } t>t_i\end{cases}$$

We further assume that the induction time for nucleation is very short compared to t_i, so that we may put $J(t)=J_s$. A well-known theorem for convolution integrals, eqn. (21), gives eqn. (22). This

$$M(t)=\int_0^t J(t_o)m(t-t_o)\mathrm{d}t_o=\int_0^t J(t-t_o)m(t_o)\mathrm{d}t_o \qquad (21)$$

$$M(t)=J_sA\int_{t_i}^t (t_o-t_i)^3\mathrm{d}t_o=\frac{1}{4}J_sA(t-t_i)^4 \qquad (22)$$

expression agrees perfectly with our observation.

In the first study,[1] in which unsieved brushite was used and supersaturation was not constant, no discontinuities in t_i were found, but inverse proportionality between t_i and $[PO_4^{3-}]^2$ was observed. As a matter of fact, a plot of ln t_i against ln $[PO_4^{3-}]$ using the results of the present study will also yield a slope of exactly -2 if we neglect points with ln $\beta>9.2$. Since there is no apparent way to explain the stepwise variation of t_i on the basis of the mechanism proposed in Ref. 2, this must be considered as purely accidental.

Some of the results reported in this paper were presented at the 2nd European Conference on Crystal Growth at Lancaster, U.K., September 1979, on the poster "Crystallization of some Constituents of Human Lithiasis" by F. Abbona, D. Aquilano, M. Franchini, C. Rinaudo, R. Boistelle, and H. E. Lundager Madsen.

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