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Dissolution rate of apatite powders in acidic fluoride solutions and the relationship to hydroxyapatite disk and bovine enamel behavior

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Summary

The dissolution kinetics of synthetic hydroxyapatite (HAP) and carbonate-containing HAP powders have been studied in fluoride-containing acetate buffer solutions partially saturated with respect to HAP ($K_{FAP} = 10^{-115}$ to 10^{-123}). The experimental results indicate that in the case of HAP powders the dissolution rates become very slow when the K_{FAP} values of the dissolution medium are larger than 10^{-119}. For the carbonate-containing apatites, however, there is a significant dissolution in the region $10^{-115} \geq K_{FAP} \geq 10^{-119}$ which is in the region of physiological and therapeutic significance.

The present results with the HAP powder together with HAP pellet data show that the dissolution of HAP pellets in the region $10^{-114} > K_{FAP} > 10^{-119}$ results from an extended transient period rising from sustained deposition of F^- on the surface and at intermediate depths in the 'lesion'. Similar effects have also been observed with bovine teeth dissolution in acidic F^- solutions.

Introduction

Studies with bovine teeth and compressed hydroxyapatite (HAP) pellets were recently completed (Fox et al., 1983; Fawzi, 1976; Bergstrom et al., 1983), which delineate conditions for remineralization only, and for simultaneous demineralization and remineralization during reaction of the HAP pellet (or bovine tooth) in

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acetate buffers containing fluoride. One of the important findings in this study was that significant dissolution did occur in acetate buffers at pH = 4.5 when the external solution's ionic activity product $K_{FAP}(= a^{10}_{Ca^{2+}} \cdot a^{6}_{PO_4^{3-}} \cdot a^{2}_{F^-})$ was in the region $10^{-114} > K_{FAP} > 10^{-120}$ for HAP pellets and $10^{-112} > K_{FAP} > 10^{-120}$ for bovine teeth. Because previous experiments with synthetic HAP and powdered enamel (Mir and Higuchi, 1969) suggested that substantial dissolution should not have occurred under these conditions, the HAP pellets and the bovine teeth results evoked a more critical examination of factors differentiating powder versus pellet dissolution behavior. The purpose of this study was to determine the dissolution rates of synthetic HAP powders especially in the region $10^{-114} > K_{FAP} > 10^{-120}$, and to assess whether these rates may be consistent with the observed behavior of HAP pellets and bovine teeth undergoing simultaneous remineralization and demineralization.

Experimental procedure

Materials

Synthetic HAP was prepared in these laboratories based on a method which is a slight modification of the one described by Avnimelech et al. (1973). A similar sample was used recently (Higuchi et al., 1983) in a study on acid dissolution kinetics.

Carbonate-containing HAP was prepared in these laboratories using the method of Legeros et al. (1971), the carbonate content being 4.85%. The product was checked by infrared and elemental analysis.

Buffer solutions

All the chemicals used for the preparation of the buffer solutions were of

TABLE I

COMPOSITION AND ION ACTIVITY PRODUCTS FOR THE DISSOLUTION MEDIA

Ion activity product		Solution/	Concentration		
pK_{HAP}	pK_{FAP}	Ca/P ratio	T CA ($\times 10^{-3}$ M)	T P ($\times 10^{-3}$ M)	T F* ($\times 10^{-5}$ M)
133.04	123.04	1.67	2.338	1.4	5.26
131.12	121.11	1.67	3.089	1.85	5.26
129.04	119.03	1.67	4.175	2.5	5.26
127.34	117.34	1.67	5.344	3.2	5.26
125.01	115.01	1.67	7.5	4.5	5.26
135.37	123.36	1.67	1.67	1.0	52.6
133.04	121.04	1.67	2.338	1.4	52.6
131.12	119.11	1.67	3.089	1.85	52.6
129.04	117.03	1.67	4.175	2.5	52.6
127.34	115.34	1.67	5.344	3.2	52.6

* 1 ppm F = 5.26×10^{-5} M F.

analytical grade. Acetate buffer solutions, 0.10 M, were prepared by mixing the calculated amounts of acetic acid and the sodium salt. Partially saturated buffer solutions were made by adding predetermined amounts of calcium chloride and sodium dihydrogen phosphate. Predetermined amounts of sodium fluoride were also added to provide the proper fluoride concentration in the solutions. Calculated amounts of NaCl were added to give an ionic strength of $\mu = 0.5$. The pH was adjusted to 4.50 ± 0.01 using concentrated HCl or NaOH. The solution ion activity products, $K_{HAP} = a^{10}_{Ca^{2+}} a^{6}_{PO_4^{3-}} a^{2}_{OH^-}$ and $K_{FAP} = a^{10}_{Ca^{2+}} a^{6}_{PO_4^{3-}} a^{2}_{F^-}$, for these solutions were calculated by the computer program developed by Fox (1977). The compositions and the corresponding ion activity products of these different dissolution media are given in Table 1.

Powder dissolution method

The powder dissolution method used in the present work has been developed in these laboratories (Higuchi et al., 1983). It was shown that when appropriate crystallite or crystallite aggregate sizes and suitable hydrodynamics are employed in suspension dissolution experiments, the crystal surface microenvironmental conditions are well approximated by the bulk solution conditions. The dissolution rate may then be simply related directly to the bulk (or external) solution conditions.

The same experimental set-up was used as previously described (Higuchi et al., 1982). Although ultrasonic irradiation seemed to have little effect on the dissolution rate under partial saturation conditions, the suspension was sonicated prior to each run in order that crystals or crystal aggregates would be predominantly in the 1 μm or less size range (Higuchi et al., 1983).

Procedure

The HAP powder aggregates were broken down by light grinding and sieving through a no. 150 mesh sieve. The exact amount of powder was suspended in 12.5 ml double-distilled water. The slurry was stirred for 18 s at 600 rpm to wet the powder and to facilitate the sonication procedure. The slurry was then sonicated for 60 s to produce a milky suspension. Stirring was resumed and 12.5 ml double-concentrated buffer solution was added at 312 s. Samples of 0.5 ml were withdrawn at suitable time intervals and immediately filtered through a Millipore membrane (GSU) filter with pore size of 0.22 μm. The filtrate was analyzed for phosphate. At certain time intervals 2 ml samples were taken for fluoride concentration measurements. All dissolution experiments were carried out at 30°C.

Analytical procedure

Phosphate concentration was determined by a colorimetric procedure described by Gee et al. (1954). The phosphoammonium molybdate complex formed was reduced by stannous chloride. The absorbance of the resulting color was determined at the end of 15 min at $\lambda = 720$ nm.

Results

Typical raw data giving the amount dissolved (ppm phosphate) versus time are shown in Figs. 1–4. It is seen that with both the HAP experiments and the carbonate-containing HAP (designated C-HAP, hereafter) the rates decrease with increasing K_{FAP} of the initial solution. The initial rates are seen to decrease to low values near pK_{FAP} of 119 and 115 for HAP and C-HAP, respectively.

Quantitative estimates of the initial rates were somewhat difficult to make, because of the high degree of curvature in the data plots (Figs. 1–4) near zero time (~ 325 s on the abscissa). For the HAP experiments, initial slopes were estimated by extrapolating the linear portions of the early time data (see dotted lines in Figs. 1 and 2). For the C-HAP experiments the best smoothed curves (see curves in Figs. 3 and 4) were used to estimate the initial rates (tangent lines to the curves in the region, 0–10 ppm phosphate). Plots of these initial rates versus the phosphate concentration of the initial solution are given in Figs. 5 and 6. The phosphate concentration is a convenient measure of the degree of partial saturation (Higuchi et al., 1983) of the initial solution and the approximate linearity of these plots show

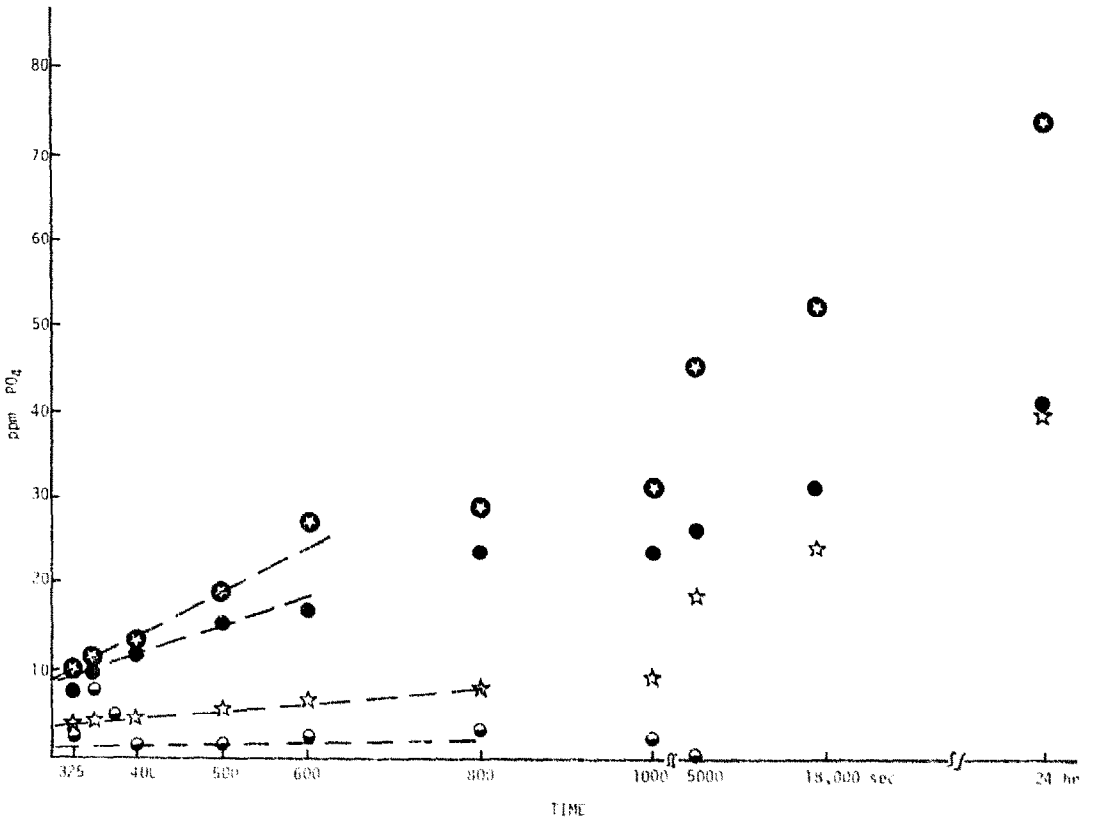

Fig. 1. Dissolution of 10 mg synthetic HAP in 0.1 M acetate buffer at pH 4.5, ionic strength $\mu = 0.5$, and 1 ppm F. Key: pK_{FAP} = ◘, 123; ●, 121; ☆, 119; ◒, 117.

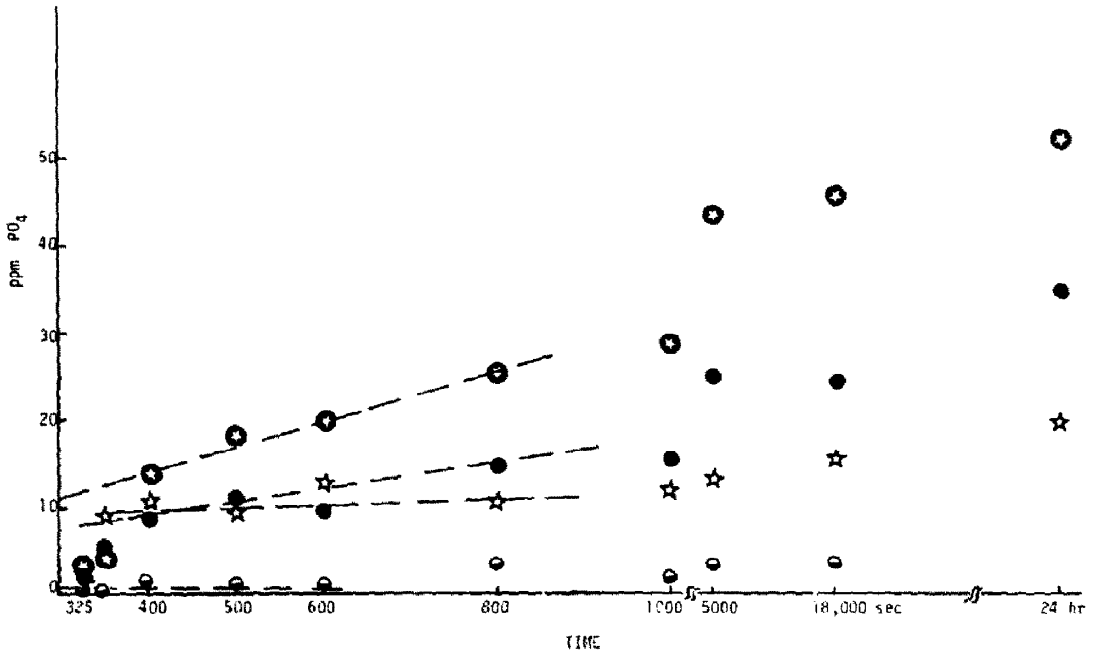

Fig. 2. Dissolution of 10 mg synthetic HAP in 0.1 M acetate buffer at pH 4.5, ionic strength $\mu = 0.5$, and 10 ppm F. Key: pK_{FAP} = ⊙, 123; ●, 121; ☆, 119; ◒, 117.

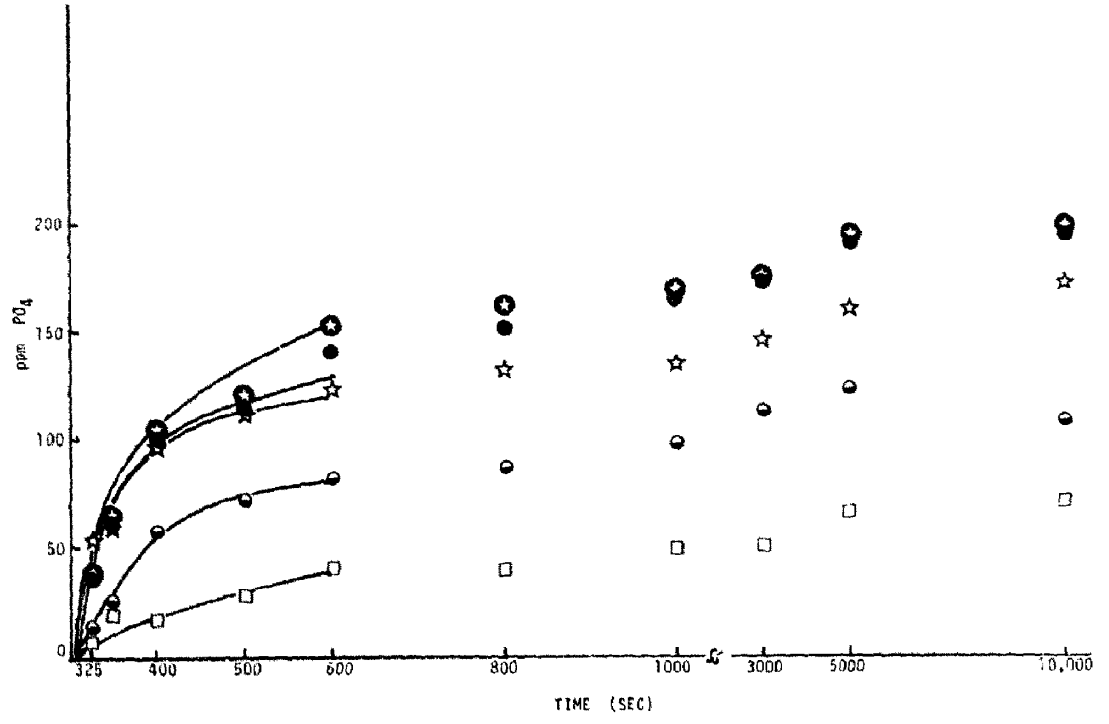

Fig. 3. Dissolution of 20 mg carbonate-containing HAP in 0.1 M acetate buffer at pH 4.5, ionic strength $\mu = 0.5$, and 1 ppm F. Key: pK_{FAP} = ⊙, 123; ●, 121; ☆, 119; ◒, 117; □, 115.

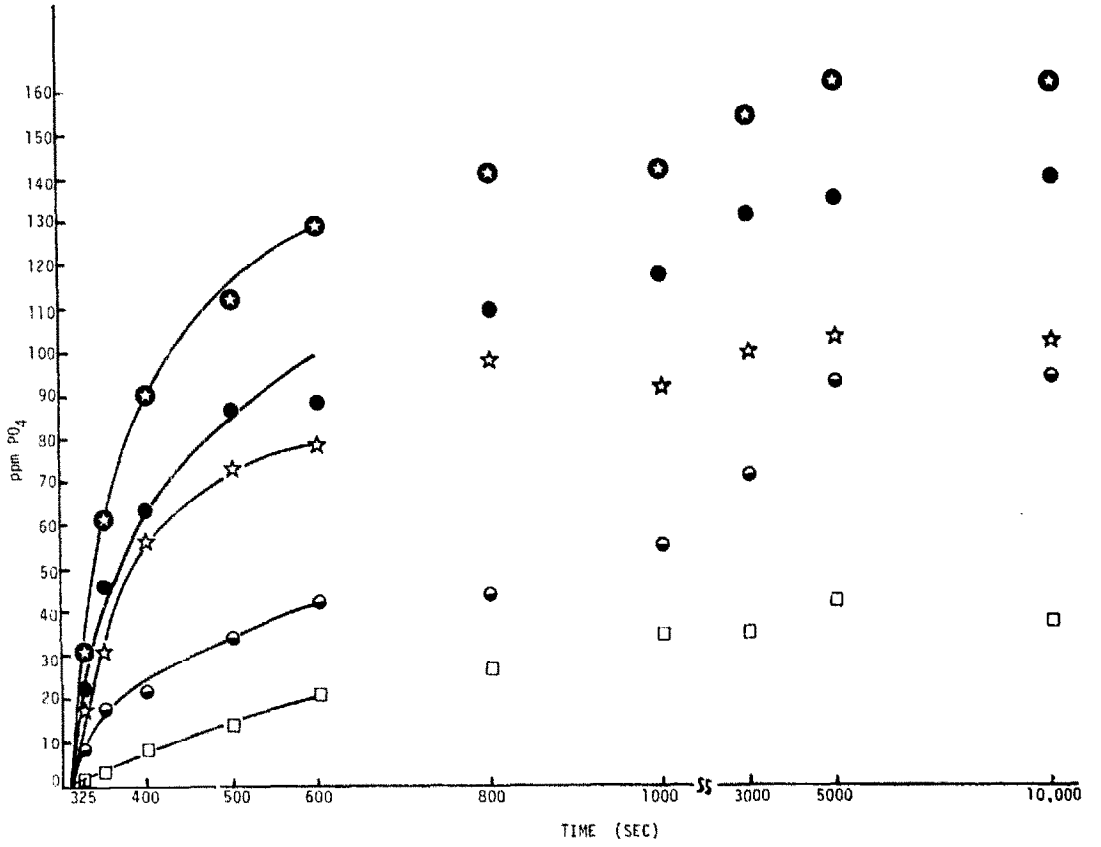

Fig. 4. Dissolution of 20 mg carbonate-containing HAP in 0.1 M acetate buffer at pH 4.5, ionic strength $\mu = 0.5$, and 10 ppm F. Key: pK_{FAP} = ✪, 123; ●, 121; ☆, 119; ◒, 117; □, 115.

that a first-order relationship,

$$\text{rate} = k \cdot \Delta C \qquad (1)$$

is obeyed reasonably well for both C-HAP and for HAP. Here ΔC is the unsaturation expressed in units of mol/liter (Higuchi et al., 1983) of the appropriate apatite and k is a first-order rate constant.

When the intercept values on the abscissas of these plots are used to calculate the corresponding K_{FAP} ion activity products at which the rates are essentially zero, it is found that $pK_{FAP} = 115.0 \pm 0.5$ for the C-HAP experiments and $pK_{FAP} = 118.5 \pm 1$ for the HAP experiments, in good agreement with what was deduced by inspection (above). On the other hand, if the intercept phosphate concentrations are used to calculate the corresponding K_{HAP} ion activity products, there is a significant difference (2–3 in pK_{HAP}) between the 1 ppm F^- and the 10 ppm F^- experiments for both the HAP and the C-HAP cases. This is the first time, to our knowledge, that the apparent solubility and the driving force for the dissolution of a C-HAP sample is described in a quantitative way. C-HAP shows a higher dissolution rate compared to synthetic HAP in the same partially saturated solutions.

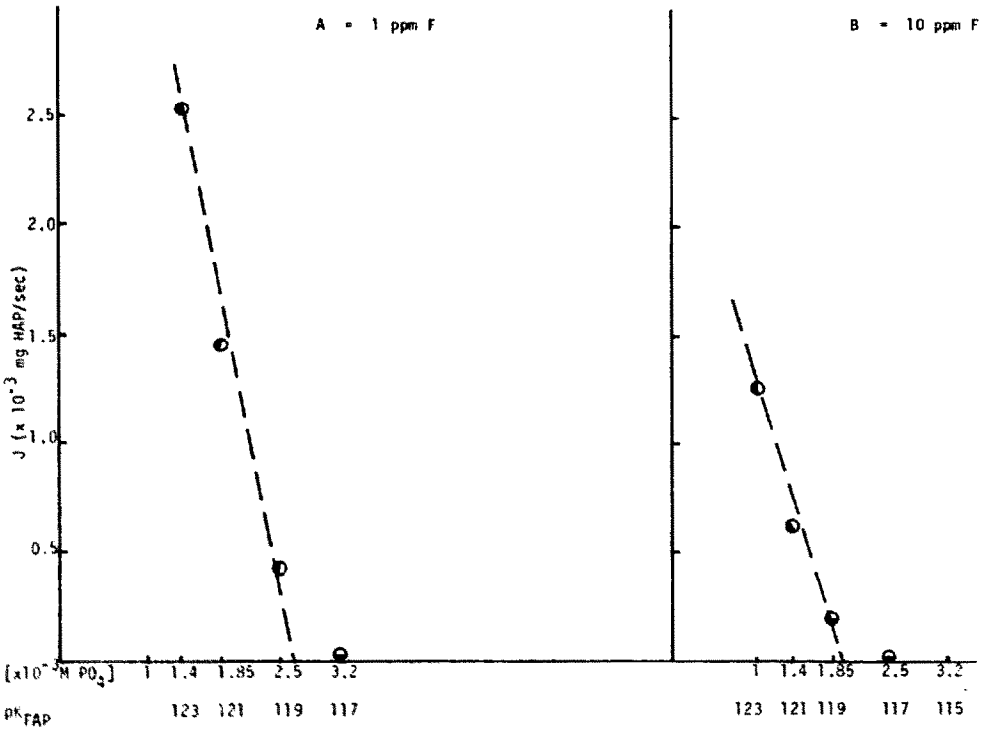

Fig. 5. Plot of J, dissolution rate, of synthetic HAP vs phosphate concentration of the initial dissolution medium. Key: A = 1 ppm F; B = 10 ppm F solutions.

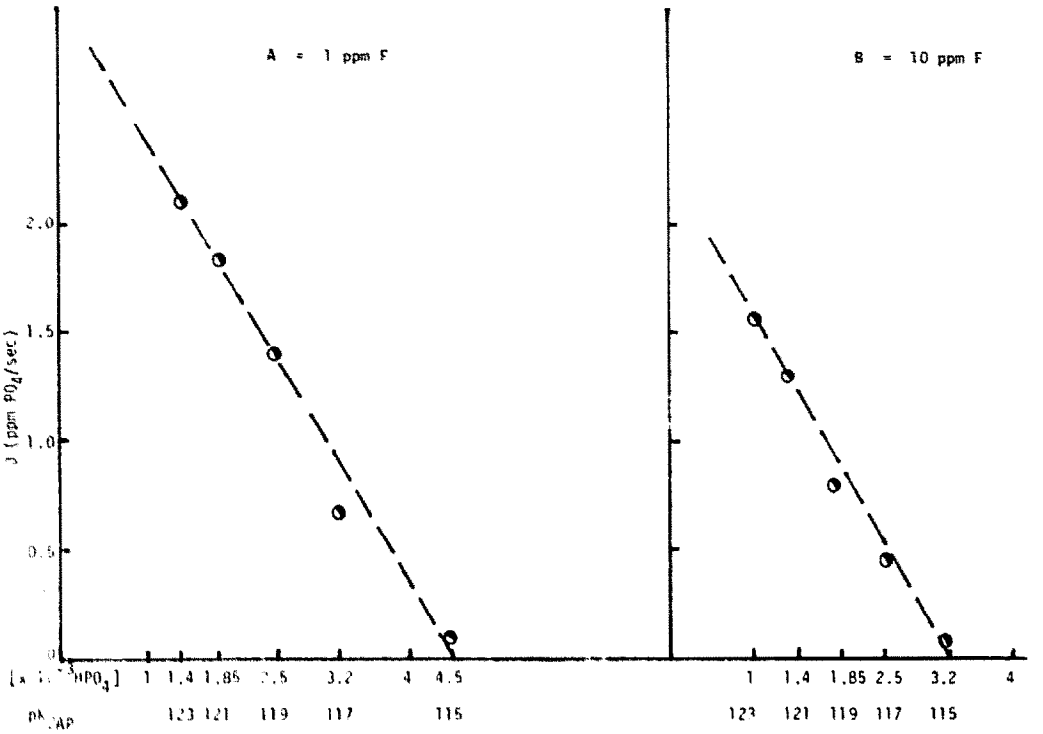

Fig. 6. Plot of J, dissolution rate, of carbonate-containing HAP vs phosphate concentration of the initial dissolution medium. Key: A = 1 ppm F; B = 10 ppm F solutions.

The above analysis, according to Eqn. 1, shows that this greater dissolution rate is related to both a K_{FAP} effect (via the ΔC factor) and a rate constant (k) effect. The latter factor may be related to specific surface area or site density differences between the two preparations.

Because the procedure used in estimating the dissolution rates for HAP and C-HAP were different and somewhat arbitrary, it was necessary to determine whether other ways of treating the data would lead to the same conclusions. Plotting amount dissolved versus ΔC (instead of the rate versus ΔC) at t = 100 and 200 s yielded similar intercept values and the plots were approximately linear for both the HAP and the C-HAP experiments.

Discussion

K_{FAP} versus K_{HAP} as the governing function

The above results show that K_{FAP} correlates better with the dissolution kinetics of HAP and C-HAP than does K_{HAP}. A wider range of solution F^--concentration dependence would better establish this relationship; however, this is precluded for the higher F^- level (e.g. 100 ppm) by precipitation of calcium fluoride and for the lower (~ 0.1 ppm) by large variations in fluoride analyses.

The present results with HAP are consistent with earlier studies (Mir and Higuchi, 1969) on both human dental enamel powder and commercial synthetic HAP and the interpretation that HAP dissolution in the presence of solution F^- is governed by a 'surface phase' of fluorapatite which forms through the rapid exchange of surface OH^- by F^-. The results obtained with C-HAP now suggest a similar mechanism holds for this material.

Powder versus pellet versus bovine teeth

The primary purpose of this study has been to determine whether the demineralization rates found in the region, $10^{-114} > K_{FAP} > 10^{-120}$, for HAP pellets (and bovine teeth) are consistent with the powder HAP dissolution data. The following analysis shows that the dissolution rate for HAP powder (Fig. 5) in this K_{FAP} region is much lower than that expected from HAP pellet experiments under the same conditions. Fawzi (1976) found that dissolution of HAP disks proceeds in solutions similar to those of the present study up to external solution K_{FAP} value of around 10^{-114}. At a K_{FAP} of 10^{-116}, for example, Fawzi observed a dissolution rate of 4×10^{-8} g HAP/s (Fig. 31 in Fawzi, 1976). If it is assumed that the disk interior pore solution conditions are essentially the same as the external solution conditions, it is possible (Fox et al., 1978) to relate the disk dissolution rate to the intrinsic crystal dissolution rate. When this is done, assuming any reasonable rate law for the crystal surface-solution kinetics, the disk dissolution rate of 4×10^{-8} g HAP/s corresponds to a 10 mg powder dissolution rate of around 0.05 ppm phosphate/s. This value is much higher than the experimental values when $K_{FAP} \geq 10^{-119}$ (Fig. 5). This discrepancy between the HAP powder and HAP pellet experiments may be explained by steady-state (or quasi-steady-state) conditions being attained only very

slowly in the HAP disk experiments. The present data suggest that, because the solution in the pores is always unsaturated with respect to $K_{HAP} = 1 \times 10^{-120}$ in the K_{FAP} region of these experiments and because F^- is supersaturated with respect to fluoroapatite, a simultaneous HAP dissolution and FAP deposition process takes place. The F^- deposition occurs near the pellet surface and at intermediate depths. This process depletes the solution F^--levels deeper in the pellet and therefore reduces the F^--inhibition effects. This in turn enhances calcium and phosphate release in the deeper regions of the zone of reaction and significantly elevates the microenvironmental K_{FAP} values near the pellet surface, exaggerating the F^- deposition tendency and maintaining this non-steady-state situation.

In recent HAP pellet and bovine teeth studies (Fox et al., 1983) chemical analyses and X-ray microdensity experiments support the above interpretation. With bovine teeth the X-ray data show the dissolution to proceed primarily in the deeper regions of the 'lesion' and both HAP pellet and bovine teeth data show high levels of FAP or fluorhydroxyapatite depositon in the intermediate regions of the lesion. Interestingly, the levels of F^- deposition are relatively independent (especially at the intermediate depths) of the external solution K_{FAP} as may be expected from the above-proposed mechanism.

With bovine teeth, simultaneous dissolution and F^- deposition occurs even at $K_{FAP} = 10^{-112}$. This suggests that bovine teeth mineral has an apparent solubility greater than synthetic HAP by around 1×10^4 in the ion activity product. Whether this may be directly related to the higher value of K_{FAP} for C-HAP (i.e. pK_{FAP} of 115 vs 119) is an interesting question. These results of the present studies have bearing on work reported by Legeros et al. (1971). From the X-ray and infrared studies Legeros et al. (1971) proposed that the effect of carbonate is to influence the size and shape of the apatite crystals and solubility and these two factors may be related. It has been suggested that, consequently, carbonate may increase the dissolution rate thereby contributing to the susceptibility to caries (LeGeros et al., 1967).

Conclusion

The present study showed that the dissolution rates of synthetic HAP powders become very slow when the ion activity product, K_{FAP}, values of the dissolution medium are larger than around 10^{-119}. In the case of a carbonate-containing (~ 5%) apatite, however, significant dissolution was observed in the region $10^{-115} \geq K_{FAP} \geq 10^{-119}$. The data suggest that carbonate is able to reduce the inhibition effect of F^- on the dissolution of apatite powders.

The present results with the HAP powder together with HAP pellet data show that the dissolution of HAP pellets in the region, $10^{-114} > K_{FAP} > 10^{-119}$, results from an extended transient period arising from sustained deposition of F^- on the surface and at intermediate depths in the 'lesion'. Similar effects have also been observed with bovine teeth dissolution in acidic F^- solutions.

Studies with C-HAP pellets and more studies with C-HAP powders are needed to

answer questions on the roles of crystallite size and shape and carbonate content in the dissolution process. These data should go far in explaining the difference in behavior between dental enamel and synthetic apatite pellets reacting in acidic fluoride solutions.

Acknowledgement

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