

Mechanism of Fluoride Uptake by Hydroxyapatite from Acidic Fluoride Solutions: I. Theoretical Considerations

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A mathematical model for the mechanism of calcium fluoride formation on hydroxyapatite in buffered fluoride solutions is proposed. It takes into account the physical and chemical processes that occur during the reaction. With the model it is possible to evaluate a priori the fluoride uptake potential of fluoride solutions.

It is well established that fluoride plays an important role in the prevention of dental caries. Fluoridation of drinking water has been a successful public health measure in reducing the prevalence of tooth decay.¹ Beneficial results have also ensued from incorporation of stannous fluoride into a dentifrice.² Wellock and Brudevold³ and others^{4,5} have reported a reduction in carious surfaces, as compared with controls, after one or more topical applications of an acidic fluoride and phosphate solution to teeth. The tooth mineral hydroxyapatite decomposes and calcium fluoride adheres to the apatite and can serve as a source of fluoride for subsequent conversion of hydroxyapatite to fluorapatite.⁶

Recently there has been interest in the application of physical chemistry principles to hydroxyapatite, the primary mineral of teeth. Gray⁷ has studied dissolution behavior of enamel and applied kinetics to charac-

terize the system in terms of the pH and the buffer. A model for the mechanism of enamel dissolution has been proposed by Higuchi et al⁸ and has been successfully tested experimentally by a powder method⁹ as well as by a solid disk method.¹⁰ This model is based on a simultaneous diffusion and equilibrium chemical reaction in contrast to other models^{7,11-14} that are based on an empirical kinetic expression of the type: rate = (constant) (concentration). The present study is a derivation of a model that represents the physical and chemical processes by which calcium fluoride is formed from hydroxyapatite and fluoride ion.

Materials and Methods

The method used to derive the model for the mechanism of the reaction was to describe the physical and chemical processes, reduce these processes to mathematical equations, combine and solve the equations, and obtain theoretical data by calculation. The last point will be reserved for a subsequent report in which theoretical data will be compared with experimental data.

Results

STEADY STATE CONSIDERATIONS.—If a flat surface of hydroxyapatite be exposed to a stirred solution of fluoride, only the direction normal to the surface, defined as the x direction, need be considered. The physical model is depicted in Figures 1 and 2. Initially the apatite is in contact with the treating solution (Fig 1), but after a finite time calcium fluoride forms and the solid-solid boundary, $x = s$, progresses (Fig 2). Fluoride and acid diffuse into the reaction site and phosphate diffuses out as the reaction proceeds. Hill¹⁵ has shown that if the ratio of the concentration difference of the

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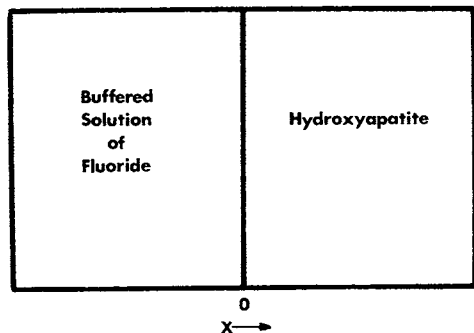


FIG 1.—Physical model for formation of calcium fluoride on hydroxyapatite shows initial situation.

diffusing species to twice the amount bound per unit volume in the new layer is sufficiently small, steady state diffusion can be assumed to exist behind the moving boundary. It can be shown that the present conditions satisfy this criterion. Thus, the steady state diffusion equations for all of the diffusing species in the region $0 \leq x \leq s$ are

$$D_{HB} \frac{d^2(HB)}{dx^2} - \phi_1 = 0 \quad (1)$$

$$D_B \frac{d^2(B^-)}{dx^2} + \phi_1 = 0 \quad (2)$$

$$D_{HF} \frac{d^2(HF)}{dx^2} - \phi_2 - \phi_6 = 0 \quad (3)$$

$$D_F \frac{d^2(F^-)}{dx^2} + \phi_2 - \phi_6 = 0 \quad (4)$$

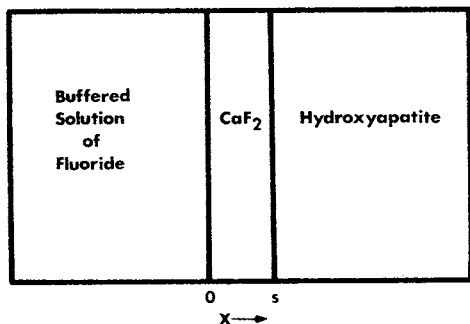


FIG 2.—Physical model for formation of calcium fluoride on hydroxyapatite as reaction progresses.

$$D_{HF_2} \frac{d^2(HF_2^-)}{dx^2} + \phi_6 = 0 \quad (5)$$

$$D_{H_3PO_4} \frac{d^2(H_3PO_4)}{dx^2} - \phi_3 = 0 \quad (6)$$

$$D_{H_2PO_4} \frac{d^2(PO_4^{2-})}{dx^2} + \phi_3 - \phi_4 = 0 \quad (7)$$

$$D_{HPO_4} \frac{d^2(HPO_4^{2-})}{dx^2} - \phi_5 + \phi_4 = 0 \quad (8)$$

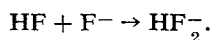
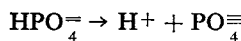
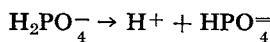
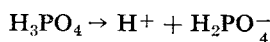
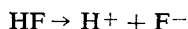
$$D_{PO_4} \frac{d^2(HPO_4^{2-})}{dx^2} + \phi_5 = 0 \quad (9)$$

$$D_H \frac{d^2(H^+)}{dx^2} + \phi_1 + \phi_2 + \phi_3 + \phi_4 + \phi_5 = 0. \quad (10)$$

The parentheses indicate the concentrations of the enclosed species and HB and B⁻ are two forms of a general buffer. The D's are effective diffusion coefficients in the heterogeneous layer of the species indicated by the subscripts. The effective diffusion coefficient is related to the diffusion coefficient of the species in the liquid by,

$$D_{\text{effective}} = D_{\text{liquid}} \frac{\epsilon}{\tau} \quad (11)$$

where ϵ and τ are the porosity and tortuosity of the heterogeneous layer. The diffusion coefficient in the liquid is assumed to be that for the binary system of the single species in the solvent. The terms ϕ_1 through ϕ_6 are, respectively, the rates of reaction per unit volume of the following reactions that take place in the region $0 \leq x \leq s$.



These rates are indeterminate as discussed by Olander.¹⁶ These terms can be eliminated by appropriate combinations of equations 1 to 10, which yield the following four equations:

$$D_{HB} \frac{d^2(HB)}{dx^2} + D_B \frac{d^2(B^-)}{dx^2} = 0 \quad (12)$$

$$D_{H_3PO_4} \frac{d^2(H_3PO_4)}{dx^2} + D_{H_2PO_4} \frac{d^2(H_2PO_4^-)}{dx^2} + D_{HPO_4} \frac{d^2(HPO_4^{2-})}{dx^2} + D_{PO_4} \frac{d^2(PO_4^{3-})}{dx^2} = 0 \quad (13)$$

$$D_H \frac{d^2(H^+)}{dx^2} + D_{HB} \frac{d^2(HB)}{dx^2} + D_{HF} \frac{d^2(HF)}{dx^2} + D_{HF_2} \frac{d^2(HF_2^-)}{dx^2} + D_{HPO_4} \frac{d^2(HPO_4^{2-})}{dx^2} + 2 D_{H_2PO_4} \frac{d^2(H_2PO_4^-)}{dx^2} + 3 D_{H_3PO_4} \frac{d^2(H_3PO_4)}{dx^2} = 0 \quad (14)$$

$$D_{HF} \frac{d^2(HF)}{dx^2} + D_F \frac{d^2(F^-)}{dx^2} + 2 D_{HF_2} \frac{d^2(HF_2^-)}{dx^2} = 0. \quad (15)$$

The first integration of equations 12 to 15 yields the following equations, respectively, where the C 's are constants of integration:

$$D_{HB} \frac{d(HB)}{dx} + D_B \frac{d(B^-)}{dx} = C_1 \quad (16)$$

$$D_{H_3PO_4} \frac{d(H_3PO_4)}{dx} + D_{H_2PO_4} \frac{d(H_2PO_4^-)}{dx} + D_{HPO_4} \frac{d(HPO_4^{2-})}{dx} + D_{PO_4} \frac{d(PO_4^{3-})}{dx} = C_2 \quad (17)$$

$$D_H \frac{d(H^+)}{dx} + D_{HB} \frac{d(HB)}{dx} + D_{HF} \frac{d(HF)}{dx} + D_{HF_2} \frac{d(HF_2^-)}{dx} + D_{HPO_4} \frac{d(HPO_4^{2-})}{dx} + 2 D_{H_2PO_4} \frac{d(H_2PO_4^-)}{dx} + 3 D_{H_3PO_4} \frac{d(H_3PO_4)}{dx} = C_3 \quad (18)$$

$$D_{HF} \frac{d(HF)}{dx} + D_F \frac{d(F^-)}{dx} + 2 D_{HF_2} \frac{d(HF_2^-)}{dx} = C_4. \quad (19)$$

Fick's first law of diffusion for the flux, J , per cross-sectional area per unit time of a substance of concentration c , is

$$J = -D \frac{dc}{dx} \quad (20)$$

Thus, physical significance can be ascribed to the constants of integration in equations 16 to 19.

$$-C_1 = J_{buffer} \quad (21)$$

$$-C_2 = J_{total\ phosphate} \quad (22)$$

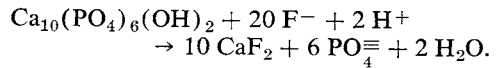
$$-C_3 = J_{total\ acid} \quad (23)$$

$$-C_4 = J_{total\ fluoride}. \quad (24)$$

Since the buffer does not take part in the chemical reaction per se, the net flow of buffer is zero:

$$J_{buffer} = 0. \quad (25)$$

Restrictions on equations 22 to 24 can be deduced from the stoichiometry of the net reaction:



These restrictions are

$$20 J_{total\ phosphate} = -6 J_{total\ fluoride} \quad (26)$$

$$20 J_{total\ acid} = 2 J_{total\ fluoride}. \quad (27)$$

Combining equations 16, 21, and 25 and eliminating the dx term by multiplying both sides of the equation by it

$$D_{HB} d(HB) + D_B d(B^-) = 0. \quad (28)$$

Combining equations 18, 19, 23, 24, and 27 and eliminating dx

$$D_H d(H^+) + D_{HB} d(HB) + D_{HF} d(HF) + D_{HF_2} d(HF_2^-) + D_{HPO_4} d(HPO_4^{2-}) + 2 D_{H_2PO_4} d(H_2PO_4^-) + 3 D_{H_3PO_4} d(H_3PO_4) = \frac{2}{20} D_F d(F^-) + \frac{2}{20} D_{HF} d(HF)$$

$$+ \frac{4}{20} D_{\text{HF}_2} d(\text{HF}_2^-). \quad (29)$$

Combining equations 17, 19, 22, 24, and 26 and eliminating dx ,

$$\begin{aligned} & D_{\text{PO}_4} d(\text{PO}_4^{\equiv}) + D_{\text{HPO}_4} d(\text{HPO}_4^-) \\ & + D_{\text{H}_2\text{PO}_4} d(\text{H}_2\text{PO}_4^-) + D_{\text{H}_3\text{PO}_4} d(\text{H}_3\text{PO}_4) \\ & = -\frac{6}{20} D_{\text{F}} d(\text{F}^-) - \frac{6}{20} D_{\text{HF}} d(\text{HF}) \\ & - \frac{12}{20} D_{\text{HF}_2} d(\text{HF}_2^-). \quad (30) \end{aligned}$$

The chemical reactions that occur in the diffusion path $0 < x < s$ obey the following concentration ionization constant expressions:

$$K_{\text{HF}} = \frac{(\text{H}^+)(\text{F}^-)}{(\text{HF})} \quad (31)$$

$$K_{\text{HB}} = \frac{(\text{H}^+)(\text{B}^-)}{(\text{HB})} \quad (32)$$

$$K_{\text{P}} = \frac{(\text{H}^+)(\text{H}_2\text{PO}_4^-)}{(\text{H}_3\text{PO}_4)} \quad (33)$$

$$K_{2\text{P}} = \frac{(\text{H}^+)(\text{HPO}_4^-)}{(\text{H}_2\text{PO}_4^-)} \quad (34)$$

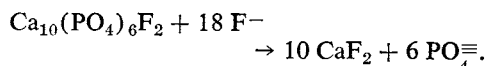
$$K_{3\text{P}} = \frac{(\text{H}^+)(\text{PO}_4^{\equiv})}{(\text{HPO}_4^-)} \quad (35)$$

$$K_{\text{HF}_2} = \frac{(\text{HF}_2^-)}{(\text{HF})(\text{F}^-)}. \quad (36)$$

An equation is now sought to describe the relationship between the participating entities of the chemical reaction that occurs at $x = s$. If the reaction takes place rapidly compared with the diffusion process, equilibrium can be assumed to exist between the components in solution and in the solid phases,¹⁷ i.e., solubility products are valid. It has been reported that the formation of calcium fluoride from calcium and fluoride ions occurs rapidly.¹⁸

When hydroxyapatite is in contact with a solution of fluoride, even at low fluoride concentration, it simulates the solubility

properties of fluorapatite.¹⁹ Because there are finite concentrations of fluoride at the boundary $x = s$, the solid immediately on the apatite side of the boundary may be considered fluorapatite (Fig 3). The stoichiometry of the net reaction, which has already been considered, is still valid for the restrictions on the diffusion equations, but the reaction that governs the equilibrium conditions at $x = s$ is



The equilibrium constant for this reaction is a combination of the solubility products of fluorapatite and calcium fluoride

$$K_{\text{eq}} = \frac{K_{\text{FAP}}}{K_{\text{CaF}_2}^{10}} = \frac{(\text{PO}_4^{\equiv})_s^6}{(\text{F}^-)_s^{18}}. \quad (37)$$

The s subscript refers to concentrations at $x = s$. *FAP* refers to fluorapatite. The subscript o will refer to concentrations in the solution (presently, $x \leq 0$). A combination of equations 34, 35, and 37 yields a new constant

$$\alpha = \frac{K_{\text{FAP}}^{1/6}}{K_{\text{CaF}_2}^{10/6} K_{3\text{P}} K_{2\text{P}}} = \frac{(\text{H}_2\text{PO}_4^-)_s}{(\text{F}^-)_s^3 (\text{H}^+)_s^2}. \quad (38)$$

The line integrals from concentrations at $x = 0$ to concentrations at $x = s$ of equations 28, 29, and 30 are combined with equations 31 to 36 and 38 to yield two equations in two unknowns

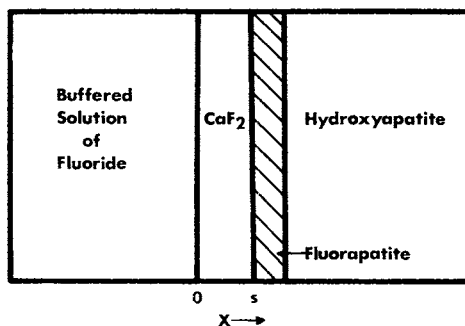


FIG 3.—Physical model for formation of calcium fluoride on hydroxyapatite with fluorapatite as an intermediate phase.

$$(F^-)_s = \frac{(QU - MV) + \sqrt{(MV - QU)^2 - 4(LV - PU)(NV - RU)}}{2(LV - PU)} \quad (39)$$

$$\begin{aligned} \kappa(F^-)_s^3(H^+)_s^2V - P(F^-)_s^2 - Q(F^-)_s - R \\ = 0 \quad (40) \end{aligned} \quad + D_{HPO_4} \frac{K_{2P}}{(H^+)_s} + D_{PO_4} \frac{K_{3P}K_{2P}}{(H^+)_s^2}$$

where,

$$L = -\frac{16}{20} D_{HF_2} \frac{K_{HF_2}}{K_{HF}} (H^+)_s$$

$$M = \frac{2}{20} D_F - \frac{18}{20} D_{HF} \frac{(H^+)_s}{K_{HF}}$$

$$N = -\frac{2}{20} D_F(F^-)_o + \frac{18}{20} D_{HF}(HF)_o$$

$$+ \frac{16}{20} D_{HF_2}(HF_2^-)_o - D_H(H^+)_s$$

$$+ D_H(H^+)_o$$

$$- D_{HB} \frac{D_{HB}(HB)_o + D_B(B^-)_o}{D_{HB} + \frac{D_B K_{HB}}{(H^+)_s}}$$

$$+ D_{HB}(HB)_o + D_{HPO_4}(HPO_4^-)_o$$

$$+ 2 D_{H_2PO_4}(H_2PO_4^-)_o$$

$$+ 3 D_{H_3PO_4}(H_3PO_4)_o$$

$$P = -\frac{12}{20} D_{HF_2} \frac{K_{HF_2}}{K_{HF}} (H^+)_s$$

$$Q = -\frac{6}{20} D_F - \frac{6}{20} D_{HF} \frac{(H^+)_s}{K_{HF}}$$

$$R = \frac{6}{20} D_F(F^-)_o + \frac{6}{20} D_{HF}(HF)_o$$

$$+ \frac{12}{20} D_{HF_2}(HF_2^-)_o + D_{H_3PO_4}(H_3PO_4)_o$$

$$+ D_{H_2PO_4}(H_2PO_4^-)_o + D_{HPO_4}(HPO_4^-)_o$$

$$+ D_{PO_4}(PO_4^{3-})_o$$

$$U = \frac{D_{HPO_4}K_{2P}}{(H^+)_s} + 2 D_{H_2PO_4}$$

$$+ 3 D_{H_3PO_4} \frac{(H^+)_s}{K_P}$$

$$V = \frac{D_{H_3PO_4}(H^+)_s}{K_P} + D_{H_2PO_4}$$

INITIAL RATE EQUATION.—If the diffusion coefficients of the three species in equation 19 are assumed to be equal, then equations 19 and 24 can be combined to give an equation for the flux of total fluoride per unit area,

$$J_{\text{total fluoride}} = -D \frac{d(TF)}{dx} \quad (41)$$

where *TF* is the sum of the hydrofluoric acid, fluoride, and twice bifluoride.

According to the liquid film theory, when the surface of apatite is exposed to the solution, a thin film of liquid exists adjacent to the apatite across which the reactants and products move. If the thickness of this film be defined as *h*, then the diffusion path at any time is from *-h* to *s* (Fig 4). For an initial rate, *s* = 0, so integration of equation 41 yields

$$J_{\text{total fluoride}} = D \frac{(TF)_i - (TF)_s}{h} \quad (42)$$

In this case *D* is the diffusion coefficient in the homogeneous liquid and it need not be corrected for porosity and tortuosity. The subscript *i* refers to initial concentration in the solution.

TIME DEPENDENT EQUATION.—Integration of equation 41 from the total fluoride con-

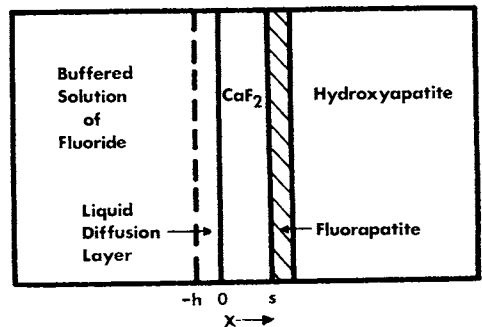


FIG 4.—Physical model for formation of calcium fluoride on hydroxyapatite including a liquid diffusion layer.

centration (TF) at $x = -h$ to that at $x = s$ gives

$$J_{\text{total fluoride}} = -AD \frac{(TF)_s - (TF)}{s + \frac{h\epsilon}{\tau}} \quad (43)$$

where A is the area of apatite exposed to the solution. The h had to be multiplied by the quantity ϵ/τ as, recalling equation 11, the D in equation 43 is the effective diffusion coefficient for the heterogeneous layer $0 \leq x \leq s$ and the $-h \leq x \leq 0$ region is the homogeneous liquid layer. The amount of fluoride lost from solution after an exposure of time t is

$$v\{(TF)_i - (TF)\} \quad (44)$$

where v is the volume of the fluoride solution. Also, the amount of fluoride lost is the time integral of the flux of fluoride,

$$\int_0^t J_{\text{total fluoride}} dt = -AD \int_0^t \frac{(TF)_s - (TF)}{s + \frac{h\epsilon}{\tau}} dt. \quad (45)$$

Combining equation 44 with the right side of 45 and taking the derivative with respect to time

$$v \frac{d(TF)}{dt} = AD \frac{(TF)_s - (TF)}{s + \frac{h\epsilon}{\tau}}. \quad (46)$$

The term s can be related to (TF) by equating the amount lost from solution with the amount deposited in the calcium fluoride layer.

$$v\{(TF)_i - (TF)\} = \frac{As\Delta(1 - \epsilon)}{19}. \quad (47)$$

Δ is the density of fluoride in pure calcium fluoride. The amount of fluoride in solution in the pores of the layer is much smaller and is omitted. Solving equation 47 for s , substituting this into equation 46, and integrating from the initial concentration to that at time t

$$\left[\frac{19v^2}{A^2\Delta(1 - \epsilon)D} \right] \left[(TF) - (TF)_i \right]$$

$$\begin{aligned} &+ (TF)_s \left[1 - n \frac{(TF) - (TF)_s}{(TF)_i - (TF)_s} \right] \\ &- \left[\frac{19(TF)_i v^2}{A^2\Delta(1 - \epsilon)D} + \frac{vh\epsilon}{\tau AD} \right] \\ &1 - n \frac{(TF) - (TF)_s}{(TF)_i - (TF)_s} = t. \quad (48) \end{aligned}$$

Thus TF is implicitly a function of time. For any specific TF the time can be calculated. The fluoride uptake for this time then can be calculated from equation 44.

Discussion

To calculate an initial rate or the amount of fluoride uptake with time, it is first necessary to solve the steady state, equations 39 and 40, for $(H^+)_s$ and $(F^-)_s$. Since dx was factored out and x does not appear in the steady state equations, $(H^+)_s$ and $(F^-)_s$ are independent of the length of the diffusion path. The values of $(H^+)_s$ and $(F^-)_s$ calculated from initial conditions of the fluoride solution [$(F^-)_o$, $(HB)_o$, etc] remain essentially constant during the course of a reaction. This is true for two reasons. Diffusion coefficients for inorganic ions have numerical values that are about equal. Thus, the contribution by the diffusion coefficients in the steady state equations effectively vanishes. Secondly, the subscript o terms always appear in a group within which they are related by stoichiometry, eg, R . The numerical value of any one of these groups, then, remains constant because as one term diminishes, another term (or terms) increases proportionately. Because of the lengthy and repetitious calculations required to solve equations 39 and 40 simultaneously and to compute equation 48, it is necessary to use a computer.

Certain soluble species were not included in the model. They are the complexes that calcium forms with phosphates.²⁰ In acidic solutions they typically account for less than 1% of the total dissolved calcium.

The numerical values needed to solve the equations are obtained from various sources. The concentrations of the solutes, the volume of solution, and the apatite area are particular experimental conditions. The ionization constants, solubility products, and activity coefficients can be found in chemistry handbooks. Diffusion coefficients

can also be found in handbooks, however, these numbers represent accurately determined values in two component systems. It would be expected that they would vary somewhat in a multicomponent system. It is a good practical assumption to allow all diffusing species to have the same diffusion coefficient. The effective diffusion layer thickness can be obtained by calibrating the experimental apparatus by a dissolution process with a compound of known solubility and diffusivity. The porosity and tortuosity can be estimated by an experiment involving the release of solute from one planar surface of a solution-saturated matrix.²¹

The usefulness of the proposed model is threefold. First, it serves to illustrate the processes that apparently occur during application of a fluoride to the teeth. It formalizes the relationships between the diffusion, the ionic equilibria, and the chemical reaction at the moving boundary. Second, it enables the estimation of fluoride uptake with time for a given topical fluoride preparation. Third, it offers a means to calculate initial rates of fluoride uptake for a given fluoride solution.

In the case of fluoride uptake with time, absolute accuracy may be difficult to achieve because of the assumption of equality of all of the diffusion coefficients and the dependence of the porosity and tortuosity on the state of the hydroxyapatite. In particular, it would be expected that the porosity and tortuosity of the calcium fluoride layer formed on a compressed disk of synthetic hydroxyapatite would be different from those of calcium fluoride formed on enamel. The use of initial rates to evaluate fluoride solutions circumvents the necessity of determining the porosity and tortuosity of the calcium fluoride layer. The use of one initial rate relative to another precludes the necessity of determining the effective diffusion layer thickness. Thus, it is possible to use initial rates to evaluate a priori the fluoride uptake potential of two or more fluoride solutions without doing any experimental work.

Conclusions

A physical chemical model for the mechanism of fluoride uptake by hydroxyapatite was proposed. It was derived on the bases of diffusion, ionic equilibria, and equi-

librium chemical reaction at a moving boundary. With the aid of a computer, it is possible to calculate initial rates of reaction that can be used to evaluate a priori the fluoride uptake potential of various fluoride solutions. The variables that can be examined are the fluoride concentration, phosphate concentration, pH, buffer type (pK_a), and buffer concentration. A forthcoming study will consider the comparison of experimental studies with the model.

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