**Original paper**

Dental Materials Journal 12(2): 209−218, 1993

# A Computer Simulation of the Reactions between Hydroxyapatite and Fluoride in Aqueous Acidic Solutions

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Received August 2, 1993/Accepted October 15, 1993

A precipitation reaction between hydroxyapatite (HAp) and fluoride solution was analyzed by computer simulation. The system comprised excess HAp and 0.05-0.2 M acetic buffer solutions containing 0.5-2.0 mM potassium fluoride. The amounts of HAp dissolved and calcium salts precipitated, and activities of all the species present in the solution were calculated during the process. In the systems, calcium fluoride was initially precipitated when applying the fluoride solution to HAp, followed by precipitation of fluorapatite (FAp) and re-dissolution of the previously precipitated calcium fluoride at a critical pH at which the ion activity product exceeded the solubility product of FAp. The critical pH was increased with pH of the buffer, whereas it was scarcely affected by fluoride ion concentration, and it was necessary to introduce phosphate ions in advance into the buffer for predominant precipitation of FAp in this system.

Key words: Hydroxyapatite, Thermodynamic reaction analysis, Computer simulation

## INTRODUCTION

Acid resistance of the tooth surface obtained by topical fluoride application depends upon the reaction products of tooth structure with acidic fluoride solutions. Thus, an understanding of the mechanism and kinetics of the interaction between acidic fluoride solution and tooth structure have long been of importance in dentistry. It is well known that the interaction involves a physicochemical uptake of fluoride ions into the tooth tissue[1-3], lattice ion exchange between the mineral and the solution[4-7], decomposition of tooth minerals and deposition of insoluble salts[8-11], and also that a number of ion species are responsible for the numerous reactions taking place in the system. These reactions are further complicated by their rate dependence[12,13].

While many experimental conditions have been reported, a comprehensive understanding has not yet been achieved because of the complexity of the system. For fluoride salt precipitation, the reaction model with diffusion layer proposed by Nelson and Higuchi[14] is generally accepted[15], but this model does not sufficiently account for the thermodynamic conditions that determine the direction and driving force of the reaction at the interface of solution and fluoride precipitates. The experimental evidence reported by Christoffersen *et al.*[16] suggests that the model fails to account for possibility of simultaneous precipitation of phosphate salts.

The reaction between hydroxyapatite and fluoride solution is driven essentially by the thermodynamic conditions of the system, and depends on the type of buffer solution, ionic strength, pH, and fluoride ion activities. While many physical factors are included in this system, a more detailed thermodynamic analysis is still required to understand its chemical behavior. Attia and Fuerstenau[17] also emphasized the need for considering thermodynamics in these systems.

In this paper, computational analyses were performed for the system by solving stoichiometric equations of every species present in the system based on the solid-liquid heterogeneous solution chemistry, and the effects of pH and the concentration of buffer and the fluoride concentration on precipitation reactions were studied.

## MATERIALS AND METHODS

### *Reaction model*

The model of precipitation reaction analyzed in this study comprised excess hydroxyapatite and 0.05-0.2 M acetic buffer solution containing 0.5-2.0 mM potassium fluoride. The possible reactions which may take place in this system are listed in Table 1. The reactions (1)-(2) are perfect dissociation of salts, (3)-(18) are the homogeneous equilibrium reactions, and (19)-(21) are heterogeneous equilibrium reactions between lattice ions in the solution and in the solid phases. The other calcium salts besides calcium fluoride ($CaF_2$) and fluorapatite (FAp) were not precipitated in this system.

Table 1 The possible reactions in the system and their equilibrium constants used in this study (25°C)

| No. | Reaction | pK |
|---|---|---|
| (1) | $KF \rightarrow K^+ + F^-$ | — |
| (2) | $K(CH_3COO) \rightarrow K^+ + CH_3COO^-$ | — |
| (3) | $CH_3COOH = CH_3COO^- + H^+$ | 4.75[2] |
| (4) | $H_3PO_4 = H_2PO_4^- + H^+$ | 2.15[2] |
| (5) | $H_2PO_4^- = HPO_4^{--} + H^+$ | 7.20[2] |
| (6) | $HPO_4^{--} = PO_4^{---} + H^+$ | 12.38[2] |
| (7) | $2H_2PO_4^- = (H_2PO_4)_2^{--}$ | 0.60[3] |
| (8) | $K^+ + HPO_4^{--} = KHPO_4^-$ | −1.04[4] |
| (9) | $F^- + H^+ = HF$ | −3.17[4] |
| (10) | $HF + F^- = HF_2^-$ | −0.60[5] |
| (11) | $H_2O = H^+ + OH^-$ | 14.00[2] |
| (12) | $Ca^{++} + CH_3COO^- = CH_3COOCa^+$ | −0.77[4] |
| (13) | $Ca^{++} + F^- = CaF^+$ | −1.04[4] |
| (14) | $Ca^{++} + H_2O = Ca\ (OH)^+ + H^+$ | 12.76[3] |
| (15) | $Ca^{++} + 2H_2O = Ca(OH)_2^0 + 2H^+$ | 25.21[3] |
| (16) | $Ca^{++} + H_2PO_4^- = CaH_2PO_4^+$ | −1.41[3] |
| (17) | $Ca^{++} + H_2PO^{4-} = CaHPO_4^0 + H^+$ | 4.80[3] |
| (18) | $Ca^{++} + H_2PO_4^- = CaPO_4^- + 2H^+$ | 13.10[3] |
| (19) | $Ca_{10}(PO_4)_6(OH)_2 = 10Ca^{++} + 6PO_4^{---} + 2OH^-$ | 117.2[1] |
| (20) | $CaF_2 = Ca^{++} + 2F^-$ | 10.31[2] |
| (21) | $Ca_{10}(PO_4)_6F_2 = 10Ca^{++} + 6PO_4^{---} + 2F^-$ | 121.2[1] |

1) Driessen, F. C. M. (1982), 2) Jpn. Chem. Soc. (1978), 3) Vereecke, G. (1990), 4) Driessens, F. C. M. (1990), 5) Liang, Z. and Higuchi, W. I. (1973)

The equilibrium reactions, (3)-(21), provide stoichiometric relations respectively for activities of the relevant species in the solution. Also the other stoichiometric relations are given from material balance on the species and electro-neutrality principle. We can set the number of equations equal to the number of the species present in the system. So the concentration and activity for every species were determined by solving the simultaneous algebraic equations numerically. At the same time, the amounts of precipitates were determined as a mass necessary to maintain the heterogeneous equilibrium.

Equilibrium constants used for the calculation are shown in Table 1. Ion exchange reactions between hydroxy ions in hydroxyapatite and fluoride ions in the solution are also possible, but their contribution to the system is still not clear and has been disregarded in this study.

As is considered from solution chemistry, dissolution of hydroxyapatite precedes precipitation of fluorides in this system. Thus, the pH of the solution goes up durig the reaction. Here, the calculations were performed at the pH settled stepwise as a precursor of the reaction from the pH of buffer solution itself.

*Computational procedure*

Algorithm for the computational analysis is shown in the form of a flow chart in Fig. 1. The computer program was written in BASIC and run on a personal computer*. The calculation of activity coefficients of the species were performed for all situations using Debye-Hückel's expanded equation with Kielland's constant[18] of the least inter-ion distance.

At first the amount of HAp dissolved was calculated at a pH arbitrarily set near the pH of the buffer solution, and the solution was examined to determine the occurrence of precipitation. If precipitation was established, the amount of precipitate was calculated as the quantity necessary to maintain the solid-liquid equilibrium condition, including the degree of saturation, otherwise the amount of HAp dissolved was re-calculated at increased pH values by set increments.

The calculation of the amount of HAp dissolved and the amounts of precipitates were repeated with the pH values increased stepwise, until the solution approached supersaturation with HAp. In every calculation, activities were determined using the activity coefficient solved by iterative method in the subroutine shown in Fig. 1-(B).

## RESULTS

Fig. 2 shows the amounts of HAp dissolved and the amounts of resulting precipitates of fluorides, $CaF_2$ and FAp, against the pH during the reaction, together with the degree of saturation with respect ot HAp ($DS_{HAp}$), defined here as a logarithm of ratio of the ion activity product to the solubility product. In the systems of Fig. 2, there are 0.5, 1.0, and 2.0 mM KF respectively in 0.1 M acetic buffer solution with an initial pH of 4.00. On applying the solution to HAp, HAp started to be dissolved with simultaneous precipitation of $CaF_2$. Dissolution of HAp and $DS_{HAp}$ in the three solutions were increased consistently with the pH. The amounts of $CaF_2$ precipitated reached to a maximum when HAp was dissolved

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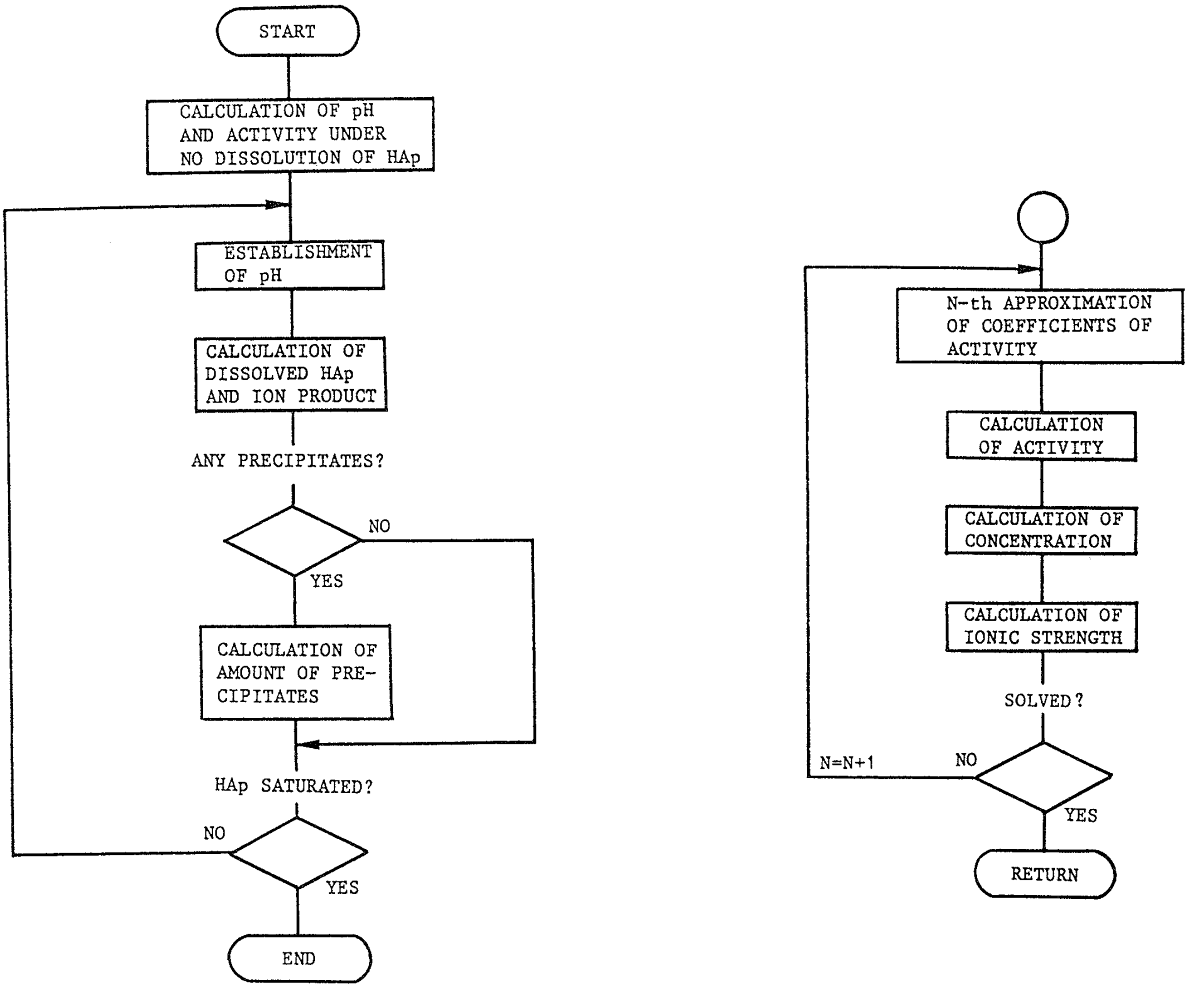


( A ) ( B )

Fig. 1 Flow chart of algorithm for the simulation (A : main routine, B : subroutine for the calculation of coefficient of activity).

less than 0.3 mM, and the maximum value was proportional to KF concentration.

At pH 5.60, FAp began to be precipitated in the solutions because the ion activity product with respect to FAp exceeded its solubility product. Simultaneously, HAp was dissolved increasingly and the previously precipitated $CaF_2$ were dissolved over. Amounts of the precipitated FAp were also proportional to KF concentration. As the pH was increased above 5.60, gradual dissolution of HAp continued without additional precipitation of FAp. In these solutions, HAp was still undersaturated even at pH 6.00.

Concentrations of the species present in the solution varied with the dissolution of HAp and the precipitation of calcium salts, as shown in Fig. 3. The buffer solution of Fig. 3 is the same as that of Fig. 2 with 1 mM KF added. Comparably highly concentrated species, except potassium cation, are shown in Fig. 3-(A). The concentrations of acetate ion, calcium ion, calcium acetate cation, and calcium fluoride cation increased with pH, while those of acetic acid and fluoric acid decreased with increase in pH. Fluoride ion sustained

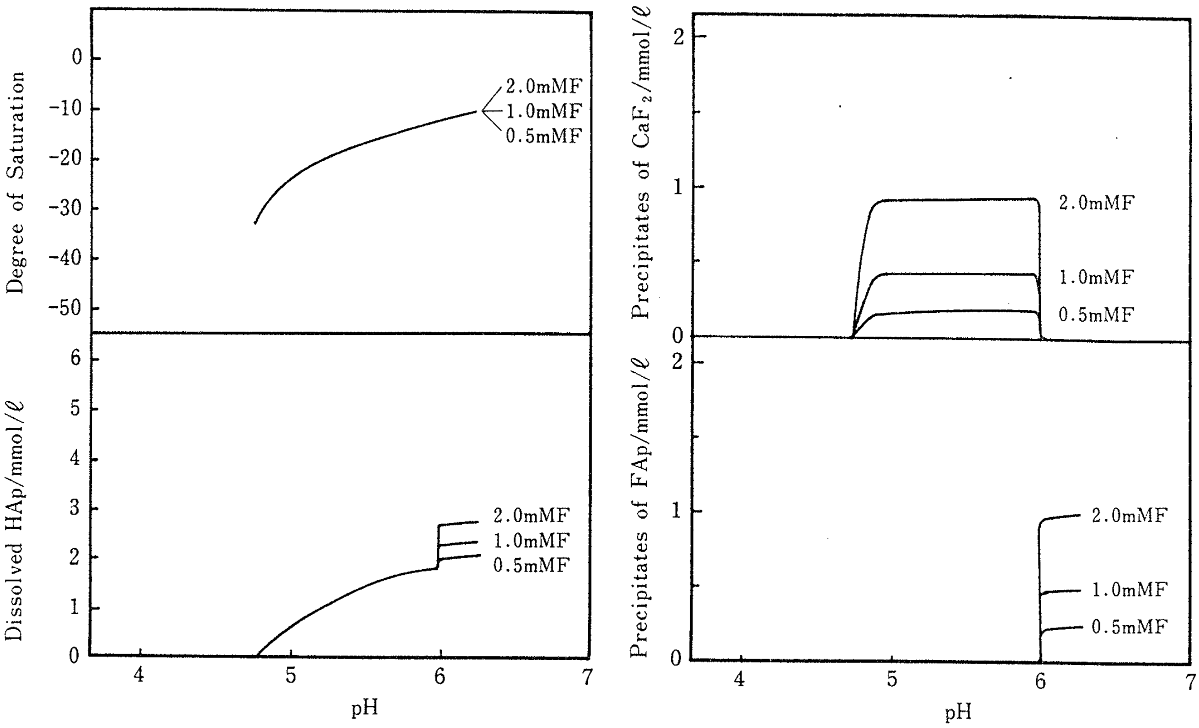
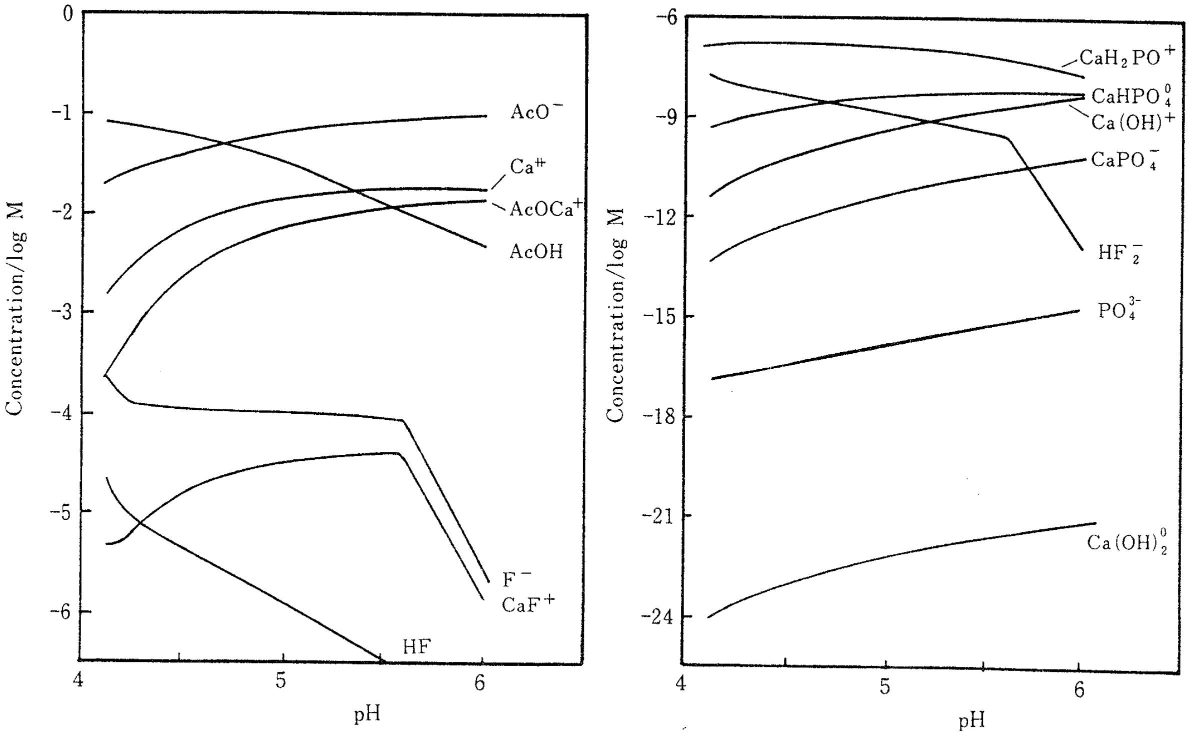


Fig. 2 The degree of saturation with respect to HAp, amounts of dissolved HAp, and amounts of precipitates of FAp and calcium fluoride in a buffer solution having a composition (initial pH 4.00 ; acetic acid 85 mM ; potassium acetate 15 mM ; potassium fluoride 0.5, 1.0, and 2.0 mM). The degree of saturation is the logarithm of ratio of ion activity product to solubility product.



(A) (B)

Fig. 3 The concentrations of species in 0.1 M acetic buffer added 0.1 mM KF with initial pH 4.00 during the reaction process.

its concentration after drastic reduction due to precipitation of $CaF_2$, until at the critical pH. The concentrations of all the fluoride species, including hydrogen difluoride anion shown in Fig. 3-(B), were decreased steeply above the critical pH, corresponding to precipitation of FAp.

Of the less concentrated species shown in Fig. 3-(B), acidic calcium phosphate cations indicated poorer changes in concentration. On the other hand, the concentration of the other species except hydrogen difluoride anion increased with the pH. These behaviors in concentration of the species did not depend upon the concentration of KF.

The $DS_{HAp}$, the amounts of HAp dissolved and the amounts of resulting precipitates of fluorides in pH 4.75 and 5.50 buffer solution with 0.1 M concentration are shown in Figs. 4 and 5. The process of the reaction in both the solutions was similar to that in the pH 4.00 solution, while the amount of HAp dissolved and the critical pH were significantly different.

As shown in Fig. 4, the critical pH was 6.00 and the amounts of dissolved HAp at the critical pH was two-thirds of that in pH 4.00 buffer solution. However, the maximum amounts of the $CaF_2$ and the FAp were almost the same. In the pH 5.50 solution, the critical pH was 6.80 and the amount of dissolved HAp at the critical pH was one-fifth of that in pH 4.00 buffer solution as shown in Fig. 5, and the maximum amounts of FAp were also less than in the other solutions, whereas the maximum amounts of $CaF_2$ were not different from the others.

Fig. 6 shows the logarithm of the amounts of HAp dissolved at the critical pH against the critical pH. The linear relations were obtained for the buffer system with same concen-

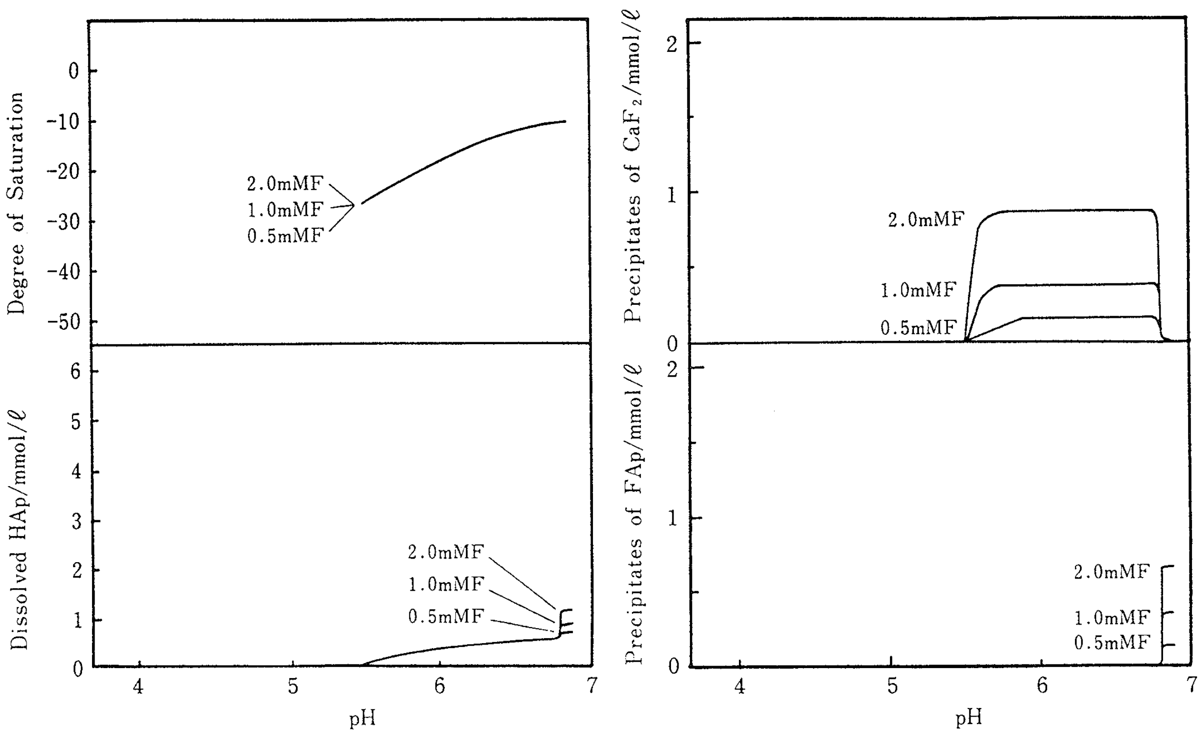


Fig. 4 The degree of saturation with respect to HAp, amounts of dissolved HAp, and amounts of precipitates of FAp and calcium fluoride in a buffer solution having a composition (initial pH 4.75 ; acetic acid 50 mM ; potassium acetate 50 mM ; potassium fluoride 0.5, 1.0, and 2.0 mM).

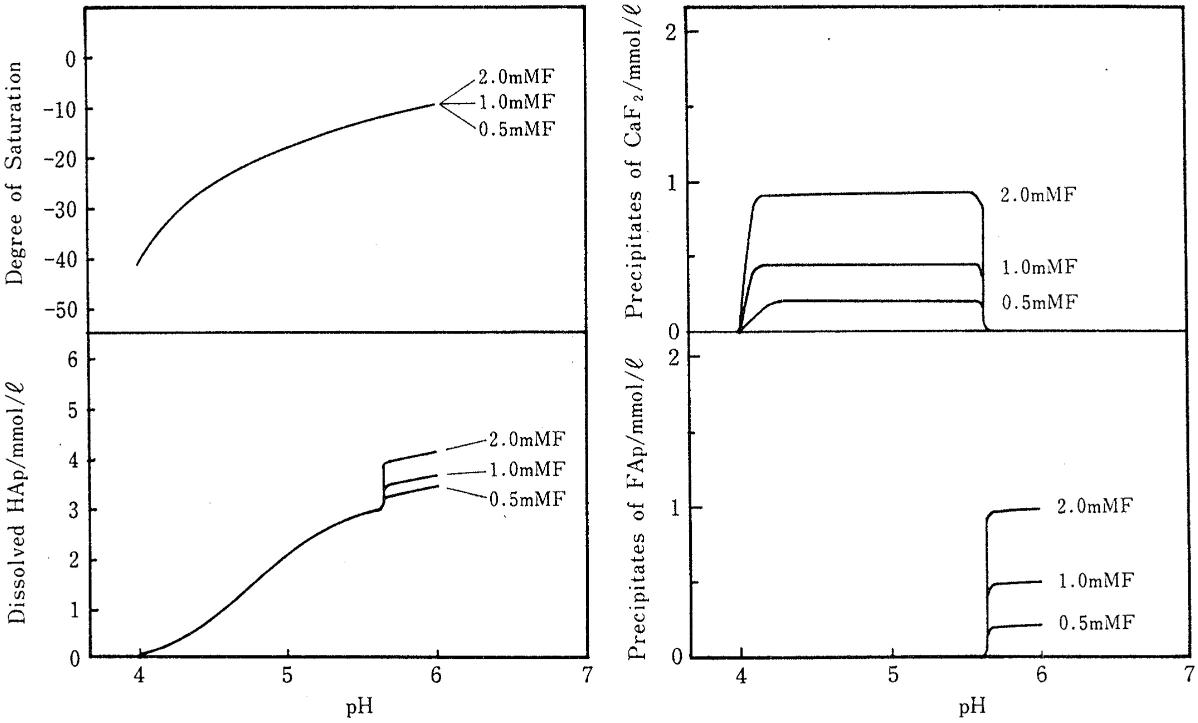


Fig. 5 The degree of saturation with respect to HAp, amounts of dissolved HAp, and amounts of precipitates of FAp and calcium fluoride in a buffer solution having a composition (initial pH 5.50 ; acetic acid 15 mM ; potassium acetate 85 mM ; potassium fluoride 0.5, 1.0, and 2.0 mM).

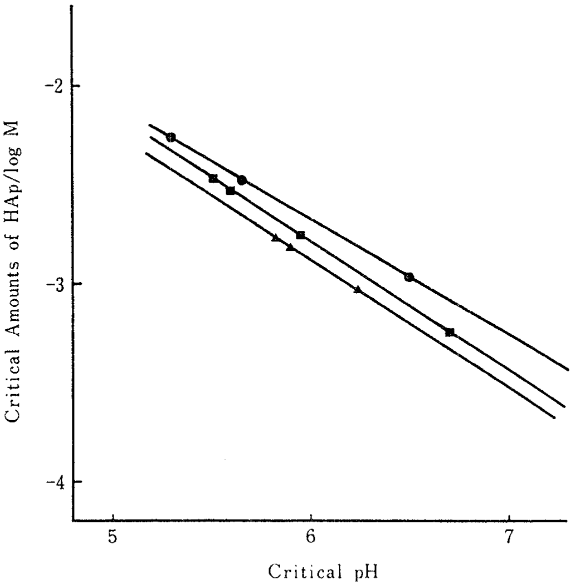


Fig. 6 The amount of HAp dissolved at the critical pH versus the critical pH in the systems of 0.2 M(●), 0.1 M(■), and 0.05M(▲), buffer solution consisting of 1 mM KF.

tration. FAp was predominantly precipitated in the range above the line. On the other hand, precipitation of $CaF_2$ was predominant in the range below the line. The line shifted up with the concentration of the buffer solution, indicating that the range in which $CaF_2$ was able to be precipitated predominantly was wide in the buffer solution with higher concentration.

## DISCUSSION

A computer simulation of the complex reaction system like this can show every chemical composition during the process and its reaction coordinates according to established thermodynamic equations. So it is useful means for us to understand the whole process.

In this analysis based on the thermodynamics, HAp starts to be dissolved prior to salt precipitation. This mechanism of the first stages of reaction seems to be supported by the reaction model reported by many workers[19-22]. The preferential precipitation of calcium fluoride in these systems is also consistent with experimental evidence[13,14,22-25].

The reason for this preferential precipitation may be interpreted theoretically using the critical condition concerned with pH of the solution and the amounts of HAp dissolved. As is well known, a salt is preferentially precipitated when the ion activity product of the salt exceeds its thermodynamic solubility product. Thermodynamic solubility products for $CaF_2$ and FAp are expressed by negative logarithmic forms as

$$pK_{CaF_2} = -\log(Ca^{++})(F^-)^2$$

$$pK_{FAp} = -\log(Ca^{++})^{10}(PO_4^{---})^6(F^-)^2.$$

Combining the above two equations to eliminate $(F^-)$ gives an equation which indicates the relation between activities of calcium ion and phosphate ion at solid-liquid equilibrium both for FAp and $CaF_2$, as follows;

$$p(K_{FAp}/K_{CaF_2}) = -\log(Ca^{++})^9(PO_4^{---})^6.$$

As stated in MATERIALS AND METHODS, all of the relevant ion activities are dependent on the quantity of HAp dissolved and the pH of solution. Thus both activities of calcium and phosphate ions in the above equation can be substituted by the equations concerned with the quantity of HAp dissolved and the pH, respectively. Consequently, we can obtain the relationship between the quantity of HAp dissolved and pH under a critical condition of solid-liquid equilibrium with respect to both FAp and $CaF_2$.

The traces of the two parameters, the quantity of HAp and the pH, divides the reaction conditions into two ranges, preferential precipitation ranges of $CaF_2$ and of FAp. The linear relationship between the two parameters was obtained by calculations as shown in Fig. 6. Calcium fluoride is preferentially precipitated below the line and FAp above the line.

The existence of the critical condition also opens the possibility of preferential precipitation of FAp in situation where fluoride ions are added to the saturated solution with respect to HAp. It is also suggested from solution chemistry that if neutral phosphate salts are added into the system, the ion activity product with respect to FAp will increase. Accordingly, FAp would be precipitated preferentially when phosphate containing fluoride solutions are applied to the mineral. This is consistent with observations by Brudevold *et al.*[19] and Larsen *et al.*[26]

The dependence of fluoride concentration on the critical condition seems to be low according to the theory, and the calculation in Figs. 2, 4, and 5 seem to bear this out. However high concentrations of fluoride ions cause increases in the quantity of precipitate, leading to an acceleration of HAp dissolution as a result of the consumption of calcium ions.

The mechanism of precipitation reaction in these systems are understood clearly from the calculation of concentration changes of every species during the reaction. There are numerous species responsible for the reaction in greater or lesser degree, because they have stoichiometric relations which are mutually dependent, their contributions to the reaction are different from one to another. The species such as $Ca^{++}$, $F^-$ , and $PO_4^{3-}$ play an important role for the precipitation as lattice ions. The other species alter the lattice ion concentration through pH change and/or material balance. Both the cations of calcium acetate and calcium fluoride, in particular, have a great effect in magnitude on the concentration of $Ca^{++}$ and $F^-$, as shown in Fig. 3. Also the pH sensitive species, for example HF, is not negligible in this calculation.

As shown above, computer simulations based on thermodynamic principles indicated the reaction coordinates in detail. It is considered that this report substantiates the theoretical mechanism of the reaction. These results will be restricted to actual reaction including rate processes. However, this program allows further analysis of the systems closer to actual case in consideration of appropriate conditions.

## CONCLUSION

A computer program has been developed for simulation of precipitation reaction of hydroxyapatite with fluorides in acidic buffer solution. The program proved to be useful in highlighting the effects of pH and fluoride concentration on the quantity of precipitates. It is therefore hoped to be a valuable tool for the reaction analysis.

## ACKNOWLEDGMENT

We thank Profs. I. Ueda, K. Matsuda, and H. Baba (Higashi-Nippon-Gakuen University) for the advice during the investigation.

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ータが完成した．

これらはCAMのための基礎データとなり得るものである．

## コラーゲン溶解能を有する根管清掃剤の象牙質とレジンとの接着性を向上させる被着面処理への応用

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著者らは，象牙質に対する接着性改善の為に，エナメル質に対する接着性が良好であることに着目し，象牙質被着面をエナメル質と化学的に同様のハイドロキシアパタイトリッチの状態とすることを試みた．この目的を達成する為にコラーゲン溶解能を持つ化合物として知られている根管清掃剤による歯面処理を試みた．

その結果は，酸系の根管清掃剤と次亜塩素酸ナトリウム系の根管清掃剤との併用が効果的であり，MとNの系で牛歯象牙質に10.7±3.9 MPa，P-SとNの系で8.8±2.2 MPaと良好な引張り接着強さを示した．さらに，これら根管清掃剤による象牙質処理面のSurface lossは従来の代表的な酸処理に較べて極めて少なく，現在，最も脱灰量の少ない部類に属するEDTAと同等またはそれ以下であった．また，処理被着面の硬度がほとんど低下していないことも大きな特徴であった．以上の結果は，根管清掃剤が歯科用レジンの象牙質に対する接着性改善に関する歯面処理剤として有効であることを示した．

## 酸性溶液中におけるヒドロキシアパタイトとフッ化物との反応に関するコンピュータシミュレーション

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合成ヒドロキシアパタイト（HAp）とフッ化物溶液との沈澱生成反応系について，コンピュータシミュレーションによる反応解析を行った．今回用いた反応系は，0.5～2 mMのフッ化カリウムを含む0.05～0.02 Mの酢酸緩衝液中に，HApを過剰に加えた系である．反応過程におけるHApの溶解量と，カルシウム塩の沈澱量ならびに系内の化学種の活量を計算した．その結果，フッ化物溶液をHApに反応させると，まずフッ化カルシウムが優先的に析出する．その後，さらにHApの溶解が進むと，FApに関してイオン活動度積がFApの溶解度積を超す臨界pH点において，FApが析出し始める．それに伴って，既に沈澱していた$CaF_2$は溶解する．

この臨界pH値は，緩衝液自身のpHが高いものほど高くなるが，フッ素イオン濃度の影響は少なかった．本系において，$CaF_2$よりもFApを優先的に析出させるためには，溶液中にあらかじめリン酸イオンを加えて，FApのイオン活動度積を高めておくことが必要であることが明らかになった．