

Resisting the Onset of Hydroxyapatite Dissolution through the Incorporation of Fluoride

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Molecular dynamics simulations of the incorporation of fluoride into hydroxyapatite show that fluoride ions are easily incorporated from solution into the surface of hydroxyapatite, but although the formation of a fluorapatite film prevents the onset of apatite dissolution, this fluoride does not segregate into the bulk material but remains at the surface. These findings significantly increase our understanding of the role of fluoride in stabilizing hydroxyapatite in tooth enamel and suggest that only repeated exposure to fluoride will have a lasting effect on the tooth enamel structure and its resistance toward dissolution and dental decay.

Introduction

Apatites $\text{Ca}_{10}(\text{PO}_4)_6(\text{F},\text{Cl},\text{OH})_2$ are a complex and diverse class of materials, which are becoming increasingly important as candidates for use as biomaterials. In the geological environment, they are the most abundant phosphorus-bearing minerals, found extensively in igneous, metamorphic, and sedimentary rocks.¹ More recently, however, they have gained additional prominence due to their biological role as one of the main constituents of mammalian bones and teeth enamel.² As such, apatites may be valuable in the manufacture of artificial bones, while another possible application is the use of ceramic implants as a support for the crystallization and layer growth of apatite, aiding the acceptance of the implant material by the body.³ Over the past decades, strengthening of tooth enamel, consisting primarily of hydroxyapatite, to prevent caries has been sought through the incorporation of fluoride into the hydroxyapatite structure, to which end fluoride was introduced in toothpaste and drinking water.⁴ The strengthening of the hydroxyapatite is thought to be due to the replacement of hydroxy groups by fluoride ions in the hydroxyapatite structure, hence promoting the formation of the less soluble fluorapatite variation,⁵ although redeposition of dissolved hydroxyapatite as less soluble fluoridated species may be even more important. However, in both cases, it is important that we obtain insight into the effect of surface fluoride species on the dissolution of the hydroxyapatite crystal and whether its presence in the surface renders hydroxyapatite more resistant towards dissolution. The present letter reports a detailed computational study of the uptake of fluoride ions from solution into the dominant surface of the hydroxyapatite crystal, followed by segregation into the sub-surface layers, as well as their resistance toward dissolution.

Theoretical Methods

Computational methods are well placed to calculate at the atomic level the energetics of fluoride uptake and distribution in the hydroxyapatite material. Our approach is to employ classical molecular dynamics (MD) techniques to study the absorption of fluoride ions from solution into the hydroxyapatite surface, thereby replacing surface hydroxy groups, followed by

diffusion of the fluoride into the bulk material. In addition, dissolution of the pure and substituted hydroxyapatite structures in water is studied to evaluate the effect of fluoride on the strength of the apatite material. We used the DL_POLY computer modeling code for the MD simulations,⁶ employing newly developed Born model potentials for the hydroxyapatite material, which were compatible with those for fluorapatite,⁷ and an established potential model for the solvent.⁸ The experimental, relative stabilities of the fluorapatite and hydroxyapatite materials and the solvated OH^- and F^- ions were accurately reproduced by the potential model, which was derived for this work from experimental enthalpies, thus ensuring that our simulations will produce reliable defect and dissolution energies. The potential parameters describing the interactions between the water molecules and the surface were obtained from scaling the F–F, O–O, and $\text{O}_w\text{--O}_w$ Buckingham potentials to the different charges and van der Waals interactions, according to the method developed by Schroder et al.⁹ The surface–water interactions used in this work were in fact taken from previous simulations of the interface between water and CaF_2 and CaCO_3 materials, which showed good agreement with both experimental results and ab initio calculations.^{10,11}

Following conventional MD simulation procedures with 3-dimensional periodic boundary conditions, the simulation cell consisted of a $2 \times 2 \times 3$ slab of hydroxyapatite crystal (20.6 Å thick) with two (0001) surfaces either side separated by a gap of 50 Å from its images in the next cell. The gap is filled with water molecules and the whole system contained approximately 2000 species in total. The simulation ensemble was NVT, i.e., a constant number of particles at constant volume and temperature, which was set at 310 K and fluctuated by less than 10 K during the data collection runs of 500 ps. Using the same potential model for water, the water density during constant pressure simulations at 300 K was found to be 1.30 g cm^{-3} . Although this value is higher than the experimental value of 1.00 g cm^{-3} , the present simulations are at constant volume with a water/vacuum interface present, rather than constant pressure simulations and the water density at the surface is hence free to vary during the simulation.

Results and Discussion

Biological apatite material has a hexagonal crystal structure, $a = b = 9.360 \text{ Å}$, $c = 6.880 \text{ Å}$, where the (0001) basal plane

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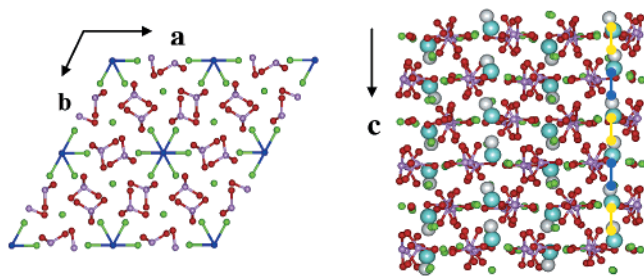


Figure 1. (a) Plan view of the fluorapatite (0001) surface, showing the F^- ions in hexagonal channels surrounded by Ca ions and (b) side view of the hydroxyapatite structure, showing regular columns of OH^- groups in the c direction ($O_{\text{phosphate}}$ = red, Ca = green, P = purple, F = dark blue, O_{OH} = pale blue, H = white, yellow O - - H distance = 2.1 Å, and blue O - - H distance = 2.8 Å).

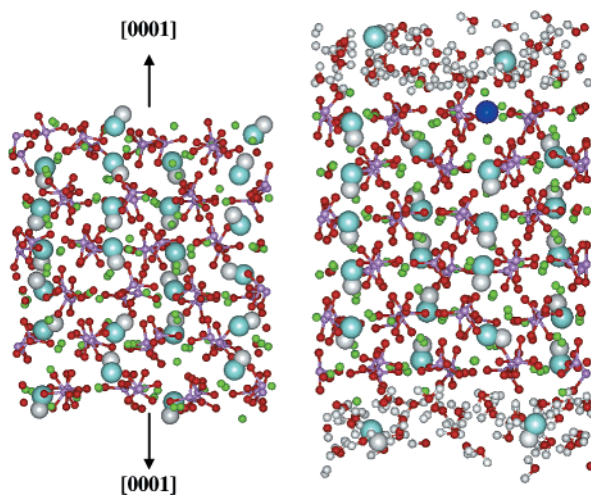
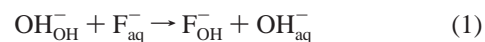


Figure 2. Side view of the slab of hydroxyapatite material (a) with two (0001) surfaces in a vacuum, showing reversal of OH^- groups in the columns and (b) in water with one surface OH^- replaced by a F^- ion, which remains in the structure while the surface OH^- groups have dissolved into the solvent water (Ca = green, F = dark blue, O_{hydroxy} = pale blue, $O_{\text{phosphate}}$ = red, O_{water} = red, H = white, and P = purple).

is the dominant surface,^{1,7} shown in Figure 1a from a bird's eye view, and we therefore concentrated on the (0001) surface in our study of the replacement of hydroxy groups by fluoride ions in hydroxyapatite. The hydroxy groups or fluoride ions in the apatite structure are all stacked above each other in hexagonal channels in the c direction, where each OH^- or F^- is bonded to three surrounding Ca ions which lie in the same a/b plane, shown in Figure 1b. Alternate rotation of the Ca positions in the a/b planes gives rise to the hexagonally shaped channels. The OH groups are stacked in a regular column within the channels, although the direction of the OH groups in the columns may differ randomly between neighboring channels.¹²

We started with a detailed investigation of the effect of introducing the surface on the OH distribution in the material. In the bulk material, we found that the OH^- groups remained lined up within the columns during the simulation, in agreement with ab initio static lattice calculations of the bulk structure where reversal of the OH^- groups within the channels was calculated to cost approximately 20 kJ mol⁻¹ per reversed OH^- group.^{12,13} However, once a vacuum gap was introduced in the simulation cell, leading to a slab of material with two (0001) surfaces either end of the slab, we found that reversal of OH^- groups occurred, leading to disordering of the OH^- groups within the channels, which is shown in Figure 2a. As we can see, though, the reversal of the OH^- groups does not take place at the surface, where all OH^- groups remain in their initial

direction, but in the OH^- positions in subsurface layers. However, a surface-vacuum interface is not a realistic model of a biological material which is at all times surrounded by fluid, and we therefore next introduced water in the simulations. With the water present at the interface the OH^- groups now remain in their bulk configuration, namely lined up in the channels without any OH^- reversals within the columns. When considering the different structures of the systems; bulk, surface/vacuum or surface/water, we observe that in the bulk material the OH^- - - O hydrogen-bond distances on average alternate between approximately 2.1 and 2.8 Å, shown for one column in Figure 1b as yellow and blue distances, respectively. As a result the OH^- groups exist in pairs, where each OH^- is closely interacting with its partner. Reversal of one OH^- group of such a pair would disrupt this close interaction through hydrogen-bonding, and this disruption would hence be energetically very unfavorable. However, in the surface-vacuum system, the pairwise structure was mainly disappeared. In the regions where some OH^- groups are still lined up, the majority of the OH^- - - O distances are now at average values of 2.3–2.5 Å and where reversal is in the process of taking place, these distances have lengthened to well over 3.0 Å; i.e., hydrogen-bonding is clearly no longer present. When water is present at the surface, the pair formation of OH^- groups remains largely intact with the OH^- - - H distances between pairs between about 2.0–2.2 Å. Hence, the driving force behind the OH^- reversals in the column of the unhydrated slab of material seems to be the absence of OH^- pair formation, which in turn is due to extensive surface relaxations of the slab of apatite material. For example, upon introduction of the vacuum gap, the calcium sublattice expands in the c direction by about 4.7% compared to the bulk material through upward relaxation of subsurface calcium ions. The calcium sublattice of the hydrated slab of material on the other hand only expands by less than 3% due to the coordination of the water shell to the surface calcium ions, which increases the coordination of the (sub-) surface calcium ions. In addition, rotation of the surface phosphate groups is also far more pronounced at the vacuum interface than in the presence of water. As a result of these extensive surface relaxations in the slab of material at the vacuum interface, the OH^- groups are pulled apart and lose their pairwise interaction, which makes them free to rotate within the column.



As we are interested in the effect of the incorporation of fluoride on crystal dissolution, we proceeded by introducing a fluoride ion at one of the hydroxy positions according to the process in eq 1, where OH_{OH}^- is a hydroxy group at a hydroxy position in the lattice and F_{OH}^- is the substitutional fluoride ion at the lattice hydroxy position. We calculated the energy of the incorporation of fluoride ions at three different positions, first at the surface but also in the second and third layers. The substitution energies are calculated using the average energies of the systems from the data collection runs. These average energies were found to vary by less than one eV (<10 kJ mol⁻¹) during the simulations, which leads to errors of less than 0.01% for the calculated substitution energies.

We found that substitution of OH^- groups by F^- ions from solution into the hydroxyapatite surface is very exothermic, releasing 193 kJ mol⁻¹ when located in the surface layer. However, incorporation into the second and third layers is progressively less exothermic, respectively releasing 164 and 68 kJ mol⁻¹, whereas subsequent segregation of fluoride further into the bulk is energetically approximately neutral at -4 kJ

mol^{-1} for the process in eq 1. It is thus relatively easy to replace surface hydroxy groups by fluoride ions, but the fluoride is not expected to penetrate deeply into the apatite material itself. As a result, whether fluoride is taken up into the hydroxyapatite material through replacement of OH groups or whether fluorapatite is formed through redeposition of dissolved hydroxyapatite material, we are left with fluorinated apatite in the surface layers only.

When water is present at the surface, the hydrated hydroxyapatite material reveals the onset of dissolution through the escape of hydroxy groups from the material into solution. However, Figure 2b shows that although OH^- groups may dissolve, the fluoride ion at the surface does not dissolve as readily but remains in the crystal. A quantitative measure of the difference in dissolution of the OH^- groups and F^- ions can be obtained from a comparison of the diffusion constants for both species. From our simulations, we calculated the diffusion constant for the fluoride ions to be zero ($0.00 \times 10^{-9} \text{ cm}^2/\text{s}$), whereas the diffusion constant for the surface OH^- groups was calculated to be $5.74 \times 10^{-9} \text{ cm}^2/\text{s}$, which is closer to the average diffusion constant for the water molecules near the surface, i.e., $1.50 \times 10^{-7} \text{ cm}^2/\text{s}$, than the subsurface OH groups at $1.23 \times 10^{-12} \text{ cm}^2/\text{s}$, clearly showing the significant movement of the surface OH^- groups in solution, which agrees with the behavior of a solvated species rather than that of a species confined in a crystal lattice. Moreover, the surface calcium ions in the pure structure also show the onset of dissolution through lengthening of the bonds to lattice oxygen ions and solvation by the surface water molecules. However, in the vicinity of the substitutional fluoride ion in Figure 2b, the calcium ions remain more closely coordinated to the material surface and the resistance toward dissolution through the incorporation of fluoride is hence 2-fold: (i) the fluoride itself remains in the material structure rather than dissolving from the lattice and (ii) it interacts with the surface calcium ions, binding them more strongly to the surface.

In this computer modeling study of the effect of fluoride on the dissolution of hydroxyapatite, we have shown that fluoride is easily incorporated into the surface from solution, but does not penetrate into the bulk material, leading to a stable thin film of fluorinated apatite. In addition, the presence of fluoride in the structure makes the material more resistant to the onset of dissolution, not only through the fluoride ions' resistance toward dissolution into the solvent, but also through their anchoring of the surface calcium ions. This study has therefore shown that the application of fluoride-containing solutions to tooth enamel, containing mainly hydroxyapatite material, will be an effective method of introducing fluoride into the structure and hence increase resistance against decay.

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Supporting Information Available: A table of potential parameters derived for this work (short-range cutoff 20 Å). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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