Atomistic mechanism of cadmium incorporation into hydroxyapatite

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Abstract

Hydroxyapatite (HAp) has been widely used to remove cadmium (Cd) in contaminated water and soils via Cd-Ca substitution. The Cd incorporation into HAp affects its structure; however, the detailed mechanism remains unclear. In this study, a series of Cd-substituted hydroxyapatites were synthesized and characterized with various techniques. Cd incorporation causes a decrease in $a$- and $c$-lattice parameters due to the radius of Cd$^{2+}$ being slightly smaller than that of Ca$^{2+}$. As the Cd content increases, the particle sizes of the synthesized samples decrease and their specific surface areas increase. Raman bands shift linearly and the $v_1$(PO$_4$) peak at 961 cm$^{-1}$ become broadened with increasing Cd content. Change in X-ray absorption near edge structure (XANES) spectra of the P K-edge indicates distortion of phosphate with Cd incorporation. Total electron yield (TEY) spectra of the Ca $L_{2,3}$-edge show a decrease in the octahedral symmetry, suggesting preferential occupancy of Cd over the Ca2 site. Extended X-ray absorption fine structure (EXAFS) analysis of the Ca K-edge reveals no obvious change in the local environment of Ca induced by Cd incorporation. However, EXAFS analysis of the Cd K-edge indicates that the substituted Cd occupies one Ca2 site in hexagonal Ca2 positions at low Cd contents (<10 mol% of Cd/(Cd+Ca)), while both Ca1 and Ca2 sites are occupied at higher Cd contents. This study provides atomistic insight into the mechanism for Cd incorporation in HAp, which will help develop an approach for effective Cd removal using HAp for environmental remediation.

Keywords: Hydroxyapatite (HAp), Cadmium, EXAFS, Raman, Incorporation mechanism
INTRODUCTION

Hydroxyapatite (HAp, Ca_{10}(PO_{4})_{6}(OH)_{2}) is one of the most common apatite-group minerals in nature, particularly important in biological systems, such as bones, teeth, and fossils (Wilson et al., 1999). HAp is also crucial in biological mineralization processes and controls the geochemical cycle of P in soils and sediments (Goldhammer et al., 2010; Zhang et al., 2010). Natural apatites commonly contain foreign cations and/or anions substituted in mineral structures because of their remarkable tolerance to structural distortion, making apatite-group minerals extremely diverse in chemical composition. Many common cations and anions have been shown to be incorporated into HAp, such as Mg^{2+}, Sr^{2+}, Mn^{2+}, Cd^{2+}, CO_{3}^{2-}, SiO_{4}^{4-}, Cl^{-}, and F^{-} (Hughes and Rakovan, 2015; Kim et al., 2017; Pan and Fleet, 2002). Among these substitutions, a large number of divalent cations have been reported to occupy Ca sites and alter the structure and properties of HAp, such as lattice parameters (Hughes and Rakovan, 2015; Lala et al., 2015; Pan and Fleet, 2002). Several cations can even form a complete solid-solution of HAp (Pan and Fleet, 2002). Such a property provides a potential in environmental applications, because the incorporation of toxic metals into mineral structure could make metals remain stable in the solid phase, thus achieving long-term remediation (Bailey et al., 2005).

Cadmium (Cd) is highly toxic and a carcinogen harmful to human health. It can be taken in human body through drinking water and nutrition, and retain in bones by replacing Ca in hydroxyapatite, which commonly causes serious “Itai-itai” disease (Kobayashi, 1978; McLaughlin and Singh, 1999). In nature, Cd usually diffuses into soils and water via atmospheric deposition, phosphate fertilizers, and sewage sludge application, causing serious Cd contamination (McLaughlin and Singh, 1999). Ca phosphate, especially HAp, is commonly used to remove heavy metals from contaminated water and soils (Bailey et al., 2005; da Rocha et al.,...
Cd can co-precipitate with Ca phosphate via isomorphic substitution, which is normally more effective than surface adsorption (Bailey et al., 2005; Valsami-Jones et al., 1998). Furthermore, phosphate has been widely used as a fertilizer for plants in soils, leading to precipitation of Cd-bearing Ca phosphate in soils (McLaughlin and Singh, 1999). Thus, mixing phosphate with metal-contaminated soils to form metal-Ca phosphate has been well established as an in-situ technique for environmental remediation (Lee et al., 2018; Skwarek and Janusz, 2016). In addition, in many phosphate ores, Cd was commonly found to be incorporated in apatite structures (Sery et al., 1996). Understanding the mechanism of Cd incorporation into HAp could help us better understand Cd geochemical behaviors and the application of HAp for Cd remediation in Cd-contaminated environment.

HAp has a hexagonal structure with space group P6₃/m (Kay et al., 1964). HAp has two nonequivalent Ca sites: Ca1 is nine O coordinated (six O-Ca in less than 2.55 Å and three more distant), while Ca2 is surrounded by seven oxygen atoms with six from five phosphates and one hydroxyl oxygen atom (Figure S1) (Laurencin et al., 2011; Sery et al., 1996). The molar ratio of Ca1 to Ca2 is 2:3, thus the chemical formula of HAp can be written as Ca₁₄Ca₂₆(PO₄)₆(OH)₂ (Zilm et al., 2016; Zougrou et al., 2016). The preferred Ca site for cation substitution and the incorporated mechanism remain unclear. Cd²⁺ can completely occupy all Ca sites in HAp and form complete solid-solutions from Ca₁₀Cd₀(PO₄)₆(OH)₂ to Ca₀Cd₁₀(PO₄)₆(OH)₂ due to their similar radii (Bigi et al., 1986; Lanfranco et al., 2003; Pan and Fleet, 2002; Zhu et al., 2016).

Thus, Cd atoms could occupy both Ca1 and Ca2 sites in HAp (Hata et al., 1978), and the substituted sites will change from one Ca site to both sites as the Cd content increases (Zhu et al., 2016). However, the concentration of Cd in soils or phosphate ores is commonly insufficient to
form pure Cd end members of HAp and only Cd-bearing Ca-HAp can be found (Bailey et al., 2005; Sery et al., 1996). Thus, understanding the site preference of Cd incorporation into HAp is helpful to understand the occurrence of Cd in phosphate-treated Cd-contaminated soils.

The occurrence of Cd in HAp has been investigated by numerous techniques, and the distribution of Cd at Ca1 and Ca2 sites is still under debate. An extended X-ray absorption fine structure (EXAFS) analysis indicates that Cd in apatite from phosphate ores occupies both Ca sites with a slight preference for the Ca2 site (Sery et al., 1996). However, other studies based on X-ray diffraction (XRD) and EXAFS analysis suggest that Cd occurs at both Ca sites without any site preference even at low Cd concentrations, and disclose a linear correlation between lattice parameters and Cd contents (Bailey et al., 2005; Lanfranco et al., 2003). It is worth noting that density functional theory calculations have shown that the Ca2 site is favored due to its more covalent properties (Tamm and Peld, 2006; Terra et al., 2010). Compared to other incorporated ions, Cd has a similar radius to Ca, resulting in small changes in lattice parameters ($a$ and $c$ from 9.42 Å and 6.86 Å to 9.32 Å and 6.65 Å, respectively for Ca and Cd end members of HAp) (Lanfranco et al., 2003). Additionally, most of EXAFS analyses have only been conducted on Cd without considering the local environment of Ca in HAp, which is also related to the occupied site preference. In this study, both Ca and Cd K-edge EXAFS analyses, total electron yield (TEY) spectra of the Ca $L_{2,3}$-edge, and X-ray absorption near edge structure (XANES) spectra of the P K-edge of synthesized Cd-substituted HAp samples with various molar ratios of Cd/(Cd+Ca) up to 0.2 were conducted to determine the effects of Cd incorporation on the local atomic environment of Ca and P in HAp, as well as to reveal the mechanism of Cd incorporation.

**MATERIALS AND METHODS**

**Synthesis of HAp and Cd-substituted HAp samples**
HAp and Cd-substituted HAp (Cd-HAp) samples were synthesized according to the reported method (Matsunaga et al., 2010), with dropwise addition of 0.1 M (NH₄)₂HPO₄ solution into a mixed solution of 0.1 M Ca(NO₃)₂·4H₂O and 0.1 M Cd(NO₃)₂. The Cd/(Cd+Ca) molar ratio of the mixed solution varied from 0.01 to 0.20, while the (Ca+Cd)/P ratio was maintained at the stoichiometric ratio of 1.67. The pH of the reaction system was kept at 10 by continuously adding ammonia solution. Obtained precipitates were aged for 48 h, then washed with distilled water, centrifuged and dried at 60 °C for 24 h. According to initial Cd/(Cd+Ca) ratios of mixed solutions, the synthesized samples were named as HAp, HAp-1Cd, HAp-5Cd, HAp-10Cd, and HAp-20Cd (Table 1).

**Characterization techniques**

The precipitates were characterized using synchrotron X-ray diffraction (XRD) at an incident energy of 18 keV with a wavelength of 0.6883 Å at beamline 14B of Shanghai Synchrotron Radiation Facility (SSRF). XRD patterns were recorded in the 2θ range of 3-45° using a line-detector model (Yang et al., 2015). Lattice parameters were refined with the GSAS software package (Larson and Von Dreele, 2000) with the EXPGUI interface (Toby, 2001). Initial unit-cell parameters for HAp were taken from Hughes et al. (1989).

The Ca, Cd, and P contents of the synthesized HAp samples were determined as follows: 10 mg of each Cd-HAp sample was digested in 10 mL of 2 M HNO₃ solution, and then Ca, Cd, and P concentrations in the solution were measured by inductively coupled plasma optical emission spectrometry (ICP-AES, Thermo Fisher Scientific 6300). The morphology of pure HAp and Cd-HAp samples (HAp-10Cd) was characterized with a high-resolution transmission electron microscope (HR-TEM, FEI TF20) operated at 200 kV acceleration voltage. Specific surface areas (SSA) were calculated using the multipoint BET method based on nitrogen adsorption
isotherms with a $p/p_0$ range of 0.05–0.20 at 77 K, which were measured on a Micrometrics ASAP 2020 apparatus after degassing at 80°C for at least 10 h. Raman spectra from 100 to 1400 cm$^{-1}$ with a resolution of 0.5 cm$^{-1}$ were collected at room temperature under a 50WL×objective of a JY/Horiba LabRAM HR Raman system with a 532.11 nm laser excitation and an 1800-groove/mm grating. Each spectrum was collected with five accumulations to improve the signal-to-noise ratio.

TEY spectra of the Ca $L_{2,3}$-edge were collected in the total electron yield mode at beamline 08U1A of SSRF. Sample powders were dispersed on an aluminum foil with a plastic support. The Ca $L_{2,3}$-edge spectra were acquired at an energy step of 0.1 eV with three averages per spectrum (Zhang et al., 2015). XANES spectra of the P K-edge and EXAFS spectra of the Ca K-edge of the synthesized samples were collected at beamline 16A1 at National Synchrotron Radiation Research Center (NSRRC, Taiwan), with an electronic storage ring of 1.5 GeV and an operating current of 360 mA. EXAFS data for the Cd K-edge in Cd-HAp samples were collected at beamline 01C1 of NSRRC. EXAFS data were processed using the Athena and Artemis from the IFEFFIT software package (Ravel and Newville, 2005). Back-scattering phase and amplitude functions were calculated with FEFF 7.02 (Ankoudinov, 1996) from the crystal structure of HAp (Hughes et al., 1989) for Ca spectra and partial Cd-for-Ca substitution for Cd spectra. Multiple scattering effects were neglected for simplification, which has already been employed in the study of Ca and Cd K-edge EXAFS spectra (Bailey et al., 2005; Harries and Hukins, 1986; Lanfranco et al., 2003; Laurencin et al., 2011).

**RESULTS**

**Characterization of the mineral phases**
The Ca, Cd, and P contents in the synthesized samples (Table 1) indicate that (Cd+Ca)/P molar ratios in all HAp samples are almost equal to the stoichiometric ratio of 1.67 and their Cd/(Ca+Cd) molar ratios are similar to those of solutions, except for HAp-20Cd, in which the Cd content is only 16.18 mol%. XRD patterns (Figure 1a) of all pure HAp and Cd-HAp samples exhibit diffraction peaks of HAp, and no other phases are present. Differences in the peak position, intensity and full width at half maximum (FWHM) of (002) are shown in Figure 1b with an enlarged XRD pattern in the range of 11° ≤ 2θ ≤ 16°, which clearly shows the shift of peak (002) to smaller d-spacing values and broader FWHM values with increasing Cd content (Figure S2). The shift is not obvious in HApS with low Cd contents (HAp-1Cd and HAp-5Cd) because of the high similarity between the radii of Cd$^{2+}$ (0.095 nm) and Ca$^{2+}$ (0.100 nm) (Shannon, 1976). Lattice parameters $a$ and $c$ decrease slightly from 9.426 Å and 6.868 Å to 9.394 and 6.824 Å, respectively (Table 1), which are linearly correlated with Cd content (Figure S3), indicating homogenous substitution (Lanfranco et al., 2003; Srinivasan et al., 2006; Terra et al., 2010). The decrease in the intensity of peak (002) and the broadening in the peak width with increasing Cd content indicate a decline in the degree of crystallization.

Table 1. Chemical compositions and refined lattice parameters

<table>
<thead>
<tr>
<th>Samples</th>
<th>Initial Cd/(Cd+Ca) (mol%) in solution</th>
<th>Cd/(Cd+Ca) (mol%) in solids</th>
<th>(Cd+Ca)/P in solids</th>
<th>SSA (m$^2$/g)</th>
<th>$a$ (Å)</th>
<th>$c$ (Å)</th>
<th>$V$ (Å$^3$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>0</td>
<td>0.00</td>
<td>1.66</td>
<td>86.1</td>
<td>9.426(2)</td>
<td>6.868(2)</td>
<td>528.44(20)</td>
</tr>
<tr>
<td>HA-1Cd</td>
<td>1</td>
<td>1.00</td>
<td>1.68</td>
<td>98.0</td>
<td>9.424(2)</td>
<td>6.864(1)</td>
<td>527.96(18)</td>
</tr>
<tr>
<td>HA-5Cd</td>
<td>5</td>
<td>4.79</td>
<td>1.68</td>
<td>100.9</td>
<td>9.412(2)</td>
<td>6.852(1)</td>
<td>525.72(18)</td>
</tr>
<tr>
<td>HA-10Cd</td>
<td>10</td>
<td>9.14</td>
<td>1.69</td>
<td>113.8</td>
<td>9.402(1)</td>
<td>6.837(1)</td>
<td>523.36(15)</td>
</tr>
<tr>
<td>HA-20Cd</td>
<td>20</td>
<td>16.18</td>
<td>1.66</td>
<td>104.6</td>
<td>9.394(1)</td>
<td>6.824(1)</td>
<td>521.51(11)</td>
</tr>
</tbody>
</table>
TEM images (Figure 2) show that all the synthesized HAp samples have spindle shapes, consistent with reported HAp crystals (Lowry et al., 2017). With an increase of Cd content in HAp, the particle sizes decrease from 50-60 nm (HAp) to <30 nm (HAp-10Cd), which explains the increase in SSA from 86.1 m$^2$/g (HAp) to 113.8 m$^2$/g (HAp-10Cd) (Table 1). The interplanar (002) spacing in HR-TEM images also decreases from 3.458 Å to 3.446 Å (Figure 2b, e), which is consistent with the (002) XRD peak’s shifting to higher 2θ values (Figure S2). The selected area electron diffraction (SAED) pattern in Figure 2c, f shows that the (221) and (222) planes have strong diffraction intensities.
Figure 2. TEM images of pure HAp (a, b, and c) and HAp-10Cd (d, e, and f). (f) displays bright rings from the SAED area (200 nm) that contains many crystals due to their small sizes.

Raman spectra and P K-edge XANES spectra of synthesized HAp

Local distortions of phosphate in the HAp structure induced by Cd incorporation are investigated by Raman spectroscopy and XANES analysis. Normalized Raman spectra of pure HAp and Cd-HAp samples (Figure 3a) and peak positions are consistent with typical bands of the HAp phase, and model assignments are compiled in Table S1 (Antonakos et al., 2017; Guerra-López et al., 2015). For all samples, the strong peak at 961 cm$^{-1}$ has been assigned to the symmetric $\nu_1$ stretching vibration of PO$_4$ groups, and peaks of three $\nu_3$(PO$_4$), three $\nu_4$(PO$_4$), and two $\nu_2$(PO$_4$) vibrations are also observed. The peak position of $\nu_1$(PO$_4$) shifts slightly down to lower wavenumbers (Figure 3b), and the FWHM values increase from 6.6 cm$^{-1}$ to 12.9 cm$^{-1}$ with increasing Cd content (Table S1), showing linear correlations with substituted Cd (Figure S4). In particular, as the Cd content increases, three peaks at ~579 cm$^{-1}$, 591 cm$^{-1}$, and 607 cm$^{-1}$ assigned
to $\nu_4(PO_4)$ vibrations show a redshift, and the intensity ratio of two peaks at 579 and 591 cm$^{-1}$ increases. All of these changes indicate an increase in progressive distortion of tetrahedral phosphate ions with Cd incorporation (Antonakos et al., 2007; Petit et al., 2017).

Figure 3. Raman spectra of pure HAp and Cd-HAp samples (a) and the magnified Raman spectra in wavenumbers of 940-990 cm$^{-1}$ (b) and 560-620 cm$^{-1}$ (c). The highest intensity of all spectra are normalized to be 1.0 for better comparison.

The P K-edge XANES spectra of pure HAp and Cd-HAp samples present the features of four peaks, consistent with reported HAp phase (Figure S5) (Liu et al., 2017). For all Cd-HAp samples, an edge jump (peak 1), a shoulder (peak 2) and two post-edge peaks (3 and 4) are at the same energy positions, exhibiting same Ca-bound P environment (Prietzel et al., 2013). However, the intensity of the shoulder related to peak 1 decreases slightly and progressively depicts an increased structural disorder of HAp with increasing Cd content, which is thought to be induced by the PO$_4$ groups bound with substituted Cd (Prietzel et al., 2013).

Ca $L_{2,3}$-edge TEY spectra of synthesized HAPs

The energy positions of the main $L_3$ ($a_2$ at ~349.4 eV) and $L_2$ peaks ($b_2$ at ~352.7 eV), as well as pre-edge peaks (hereafter called $a_1$ and $b_1$) in the Ca $L_{2,3}$-edge TEY spectra of all HAp...
samples (Figure 4) are quite similar. Commonly, the split energy of $a_1$ and $a_2$ peaks is proportional to the crystallinity of HAps (Beniash et al., 2009; Politi et al., 2008; Zougrou et al., 2016). The split energy of pure HAp and Cd-HAps are similar to each other (Figure S6, Tables S2), indicating little change in the crystallinity due to Cd incorporation, which is also shown in XRD results. For pre-edge peaks, $a_1$ has been reported to represent the octahedral ($O_h$) symmetry of Ca$^{2+}$ caused by the 2p-3d spin-orbit coupling, mainly contributed from Ca2 sites (Cosmidis et al., 2015; Naftel et al., 2001). The decrease in relative intensities ($a_1/L_3$ in Table S2) with Cd content indicates that the $O_h$ symmetry from the Ca2 site decreases with Cd incorporation, suggesting that Cd has preferentially entered this site. This interpretation relies on the assumption that the coordination environment (coordination numbers and bond distance) of Ca in each site remains the same upon Cd incorporation (Laurencin et al., 2011). Given that the local environment of Ca mainly depends on the Ca···O coordination, the average bond distance and coordination number of Ca···O in the first sphere should be similar for all HAp samples. To confirm this interpretation, EXAFS spectra of the Ca K-edge are analyzed to reveal the local environment of Ca.

![Figure 4. TEY spectra of the Ca $L_{2,3}$-edge in pure HAp and Cd-HAp samples.](image)

**EXAFS spectra of the Ca K-edge in HAps**
The Ca K-edge XANES spectra of Cd-HAp samples are nearly identical to that of pure HAp, except for a decrease in the shoulder peak intensity (Figure S7a). The XANES spectrum of HAp-20Cd with the highest Cd content is nearly identical to that of pure HAp (Figure S7b), especially in the pre-edge region, which is sensitive to the local distortion around Ca ions. The pre-edge region at 4037 eV due to the 1s→3d electron transition is similar regardless of Cd content, suggesting that the local environment of Ca atoms are similar in Cd-HAp samples (Laurencin et al., 2011; Neuville et al., 2004).

EXAFS spectra of the Ca K-edge and structural fitting of HAp samples are shown in Figure 5 and listed in Table S3. The $k^3\chi(k)$ spectra and the Fourier transforms (FT) of HAp and Cd-HAp are very similar, consistent with reported HAp spectra (Harries and Hukins, 1986; Harries et al., 1988; Laurencin et al., 2011). Their Fourier transforms show three peaks with similar intensity of the first peak at ~1.9 Å (indicated by P1 and not corrected for phase shifts) (Figure 5b), and the fitted bond distances and Debye-Waller factors ($\sigma^2$) are quite similar, suggesting that the local geometry of the nearest Ca···O shell is not significantly modified by Cd incorporation. For distant shells (>3 Å) contributed from the back-scattering of surrounding P, Ca, and more distant O (Harries and Hukins, 1986; Laurencin et al., 2011), neither the spectra nor fitting results show any noteworthy change due to Cd incorporation. For HAp-20Cd, the third peak (P3) intensity is slightly stronger than that in HAp (Figure 5b). Given that this part of the spectrum arises from Ca atoms, the increase in the P3 intensity could result from the presence of Cd atoms, which are heavier and thus have stronger back-scattering than Ca. However, it is difficult to evaluate any change in the long-range ordering around Ca due to slight difference among fitting parameters (Table S3). The low Cd content and similar ion radii of Cd$^{2+}$ and Ca$^{2+}$ hardly modify the local environment of Ca.
EXAFS spectra of the Cd K-edge in HAp samples

There is no perceptible change due to Cd incorporation in XANES spectra of the Cd K-edge in Cd-HAp samples (Figure S8), implying that the local geometries are similar regardless of Cd content in HAp. The EXAFS spectra and structural fitting results for Cd in HAp samples are shown in Figure 6 and Table 2. The Fourier transforms of $k^3\chi(k)$ in R-space also exhibit three main peaks (Figure 6b), displaying that peak 1 (P1) is identical while a small but systematic increase in peak 2 (P2) and a decrease in peak 3 (P3). In comparison with the Ca K-edge spectra in pure Ca-HAp (Figure 5b), peak 2 in the Cd K-edge spectra is more intense than peak 3. In pure Ca-HAp, peak 2 results from the contribution of Ca···P (3rd shell) and Ca···Ca (4th shell) back-scattering, which are mainly derived from Ca1 as the center atom (Table S3) (Laurencin et al., 2011). In low Cd-HAp samples (HAp-1Cd, HAp-5Cd, and HAp-10Cd), peak 2 is relatively weak, indicating that Cd is located at the Ca2 site with only three P shells back-scattering.
contributing to the low intensity of peak 2 (Lanfranco et al., 2003). However, in HAp-20Cd, the increase in the peak 2 intensity indicates that the back-scattering from Cd at the Ca1 site also contributes to this peak because Cd1 in Cd-HAp has the shortest Cd···Ca distance (Harries and Hukins, 1986). This also confirms that in the Cd-HAp end member, Cd occupies all Ca1 and Ca2 sites, and EXAFS spectra of the Cd K-edge are similar to those of the Ca K-edge in both Ca- and Cd-HAp end members, with a stronger peak 2 than peak 3 (Sery et al., 1996). Thus, because of the weaker intensity of peak 2 than that of peak 3 in Cd-HAp, we deduce that Cd preferentially occupies the Ca2 site in HAp at a low content, and the structural fittings of Cd-HAps are conducted with Cd at the Ca2 site.

The fitting parameters listed in Table 2 show that peak 1 derived from two Cd···O shells displays the shortest Cd-O distance of 2.28 Å, which is consistent with the reported shortest Ca-O distance of Ca2 sites in pure Ca-HAp (Harries and Hukins, 1986). The fitting parameters of the bond distance and Debye-Waller factor ($\sigma^2$) are quite similar in HAp-1Cd, HAp-5Cd, and HAp-10Cd. The good fit assuming that Cd is located at the Ca2 site confirms that Cd incorporates into the Ca2 site preferentially. However, the difference in the fifth shell of Cd···P in HAp-20Cd has a shorter bond distance of 3.67 Å, which is much shorter than those of HAps with low Cd contents. Since Cd at the Ca1 site has been reported to have a shorter Cd1···P distance (Laurencin et al., 2011), the back-scattering of the surrounding P of Cd1 could make fitted distance shorter. This could also result in an increase in the peak 2 intensity, suggesting that Cd atoms also occupy Ca1 sites in HAps with high Cd contents.
Figure 6. EXAFS spectra of $k^3$-weighted (a) and Fourier transform magnitudes (b) of the Cd K-edge in Cd-HAp samples. Dots are raw data and solid lines are structural fits.

### Table 2. Fitting parameters of the Cd K-edge EXAFS spectra in Cd-HAp samples with the model of Cd at the Ca$^{2+}$ site.

<table>
<thead>
<tr>
<th>Atom/shell</th>
<th>HAp-1Cd</th>
<th>HAp-5Cd</th>
<th>HAp-10Cd</th>
<th>HAp-20Cd</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$N^\dagger$ R ($\AA$)</td>
<td>$\sigma^2(10^{-2}\text{nm}^2)$</td>
<td>$N^\dagger$ R ($\AA$)</td>
<td>$\sigma^2(10^{-2}\text{nm}^2)$</td>
</tr>
<tr>
<td>O/1$^{st}$</td>
<td>5 2.28 0.008</td>
<td>5 2.29 0.008</td>
<td>5 2.28 0.009</td>
<td>5 2.28 0.009</td>
</tr>
<tr>
<td>O/2$^{nd}$</td>
<td>2 2.52 0.015</td>
<td>2 2.52 0.014</td>
<td>2 2.51 0.017</td>
<td>2 2.51 0.023</td>
</tr>
<tr>
<td>P/3$^{rd}$</td>
<td>1 3.08 0.006</td>
<td>1 3.08 0.008</td>
<td>1 3.08 0.008</td>
<td>1 3.08 0.010</td>
</tr>
<tr>
<td>P/4$^{th}$</td>
<td>2 3.38 0.025</td>
<td>2 3.37 0.028</td>
<td>2 3.42 0.032</td>
<td>2 3.37 0.028</td>
</tr>
<tr>
<td>P/5$^{th}$</td>
<td>2 3.78 0.030</td>
<td>2 3.74 0.030</td>
<td>2 3.79 0.030</td>
<td>2 3.67 0.030</td>
</tr>
<tr>
<td>Ca/6$^{th}$</td>
<td>6 3.97 0.010</td>
<td>6 3.98 0.011</td>
<td>6 3.97 0.013</td>
<td>6 3.96 0.015</td>
</tr>
<tr>
<td>Ca/7$^{th}$</td>
<td>4 4.15 0.005</td>
<td>4 4.16 0.006</td>
<td>4 4.14 0.008</td>
<td>4 4.13 0.011</td>
</tr>
</tbody>
</table>

Note: $^\dagger$ values fixed at averaged crystallographic values. Typical errors on the bond distances and Debye-Waller factors are $\pm 0.02 \text{\AA}$ in R and $20\%$ in $\sigma^2$, respectively.
DISCUSSION

Effect of Cd incorporation on the HAp crystal structure

The diffraction peaks shift and the lattice parameters \((a, c, \text{ and } V)\) linearly change with substituted Cd content, which mainly results from smaller radii of \(\text{Cd}^{2+}\) compared to \(\text{Ca}^{2+}\) (Bigi et al., 1986; Lanfranco et al., 2003). The decrease in intensity and the increase in width of the XRD peak (002) (Figure S2) indicate slightly decreased crystallinity due to Cd incorporation (Zhu et al., 2016). In contrast, several synthesized metal-substituted HAp's with \(\text{Mg}^{2+}\) and \(\text{Zn}^{2+}\) suggest that the crystallinity of substituted HAp's decreases obviously at 5% and 10% substitutions (Arul et al., 2018; Guerra-López et al., 2015), as both \(\text{Mg}^{2+}\) and \(\text{Zn}^{2+}\) have much smaller radius than \(\text{Ca}^{2+}\) \((r_{\text{Mg}^{2+}}=0.72 \, \text{Å}, \ r_{\text{Zn}^{2+}}=0.74 \, \text{Å}, \ \text{and } r_{\text{Ca}^{2+}}=1.00 \, \text{Å})\). Interestingly, sorption experiments of \(\text{Cd}^{2+}\) and \(\text{Zn}^{2+}\) on HAp also indicate that \(\text{Cd}^{2+}\) could be more easily incorporated into the HAp structure than \(\text{Zn}^{2+}\) (Xu et al., 1994).

Changes in the local environment of phosphate in HAp's due to Cd incorporation are reflected by modifications of peak position, FWHM, and intensity of Raman spectra. The redshift and broadening of \(\nu_1(\text{PO}_4)\) are linearly correlated with Cd content. The \(\nu_1(\text{PO}_4)\) mode was reported to correspond with the vibration in which \(\text{P}, \text{O1},\) and \(\text{O2}\) atoms were on the mirror plane and two \(\text{O3}\) atoms at both sides of the plane (Antonakos et al., 2007). The incorporated Cd at the Ca2 site is bound with two next-nearest O3 atoms, producing a distortion of phosphate with slight decrease in the O3-P-O3 angle due to the smaller radius of Cd and the mass difference (Hata et al., 1978; Mercier et al., 2005). The distortion of phosphate bound with Cd results in redshifts and broadening of \(\nu_1(\text{PO}_4)\), where both of them exhibit a linear relation with Cd content. The substitution of other cations in HAp was also reported to cause phosphate
distortions and induce a change in Raman spectra (Antonakos et al., 2017; Antonakos et al., 2007; Stammeier et al., 2018; Terra et al., 2009). For other substituted cations, in comparison, a 3.2 mol% Zn substitution could cause a shift of 2 cm\(^{-1}\), while the incorporated Cd with a content of 16.18 mol% only induces a 2 cm\(^{-1}\) shift, indicating that the effect of Cd\(^{2+}\) incorporation on the symmetry distortion of phosphate tetrahedron is much weaker than Zn\(^{2+}\) due to similar radii of Ca\(^{2+}\) and Cd\(^{2+}\) (Guerra-López et al., 2015; Lanfranco et al., 2003). Such effects of Cd incorporation are also indicated by the decline in \(\nu_3(PO_4)\) peaks at 1025, 1045, and 1073 cm\(^{-1}\) (Antonakos et al., 2017). However, the change induced by Cd incorporation is too slight to alter the bond length of P-O even as the Cd content reaches 16.18 mol%. In that case, the slight change only causes a small decrease in the shoulder peak (peak 2 in Figure S5) of the P K-edge XANES spectra, and the P K-edge XANES analysis might not be sensitive enough to differentiate the crystallinity of HAp with Cd incorporation (Chen and Arai, 2019). The small difference between the ionic radii of Ca\(^{2+}\) and Cd\(^{2+}\) (only 0.04 Å) only changes the structure slightly without disrupting the framework, which also contributes to the thermodynamic basis to form completely continuous solid-solutions of Ca\(_{10}\)(PO\(_4\))\(_6\)(OH)\(_2\)-Cd\(_{10}\)(PO\(_4\))\(_6\)(OH)\(_2\) (Pan and Fleet, 2002).

Site preference of Cd incorporation into HAp

Ca1 and Ca2 are crystallographically inequivalent sites in HAp, and both have the potential for substitution of foreign ions. Although the preferred Ca site for different foreign ions is still under debate, more studies have suggested that Ca2 is the preferred site based on Rietveld analysis of XRD data and first principles calculations (Guerra-López et al., 2015; Lala et al., 2015; Luo et al., 2009; Terra et al., 2010). In this study, the local environment of Ca and Cd in
HAp are investigated and the incorporation mechanism is revealed by combining Ca \(L_{2,3}\)-edge TEY, Ca K-edge EXAFS, and Cd K-edge EXAFS analysis. The surrounding atomistic environment of Ca with O is hardly altered by Cd incorporation (< 20 mol%), which has also been confirmed in the Ca K-edge spectra of Mg-substituted HAp (Laurencin et al., 2011). The similarity of the bond distance and coordination number of Ca in Cd-HAps confirms that Cd is indeed at the Ca\(_{2}\) site, as reflected in the Ca \(L_{2,3}\)-edge TEY spectra. According to Ca \(L_{2,3}\)-edge TEY spectra (Figure 4) and EXAFS spectra of the Cd K-edge (Figure 6b), we propose that Cd atoms prefer to occupy the Ca\(_{2}\) site, and the reasonable fitting of \(r_{\text{Cd-O}}=2.28\ \text{Å}\) is consistent with the Cd\(_{2}\)-O distance (2.28 Å) (Harries and Hukins, 1986). The higher electronegativity of Cd (1.7) over Ca (1.0) results in a higher preference of Cd for Ca\(_{2}\) site to increase covalent interactions with the hydroxyl oxygen bonding with Ca\(_{2}\) (Terra et al., 2010). Furthermore, theoretical calculations have shown that Cd in Ca\(_{1}\) sites largely increases variation in the Cd-O distance (Terra et al., 2010), which is opposite to the results of a similar Cd-O distance in EXAFS fitting and a linear decrease in lattice parameters of Cd-HAps with increasing Cd content (Lanfranco et al., 2003). Thus, the Ca\(_{2}\) site in HAp is preferential for Cd incorporation. However, the possible limited content of incorporated Cd that only occupies Ca\(_{2}\) sites needs to be explored.

The spatial accommodation without disrupting the framework should be a key factor to determine the site preference with different Cd contents (Pan and Fleet, 2002). From the geometrical configuration of Ca\(_{2}\) atoms in the HAp structure, two adjacent triangles (\(\triangle\), \(\nabla\)) with the nearest cations are shown to form one Ca\(_{2}\) hexagon (Figure S9 a, b). Occupancy at one Ca\(_{2}\) site in the Ca\(_{2}\) hexagon reaches a Cd content of 10 mol%. Assuming homogenous substitution of Cd without forming a Cd-Cd cluster in the HAp structure, substituted Cd should first occupy Ca\(_{2}\) sites diagonally with the longest Cd-Cd bond distance in the Ca\(_{2}\) hexagon.
(Figure S9c and d), in which the excess energy for the maximized Cd2-Cd2 distance is more negative to favor this configuration (Terra et al., 2010). Thus, Cd atoms occupying two Ca2 sites in one hexagon could reach 20 mol% of all Ca sites in HAp. However, our EXAFS analysis indicates that Cd also occupies Ca1 sites in HAp-20Cd (≥16.18 mol%), suggesting that only one Ca2 site in the Ca2 hexagon is preferentially substituted by Cd. Then, with further increasing Cd content above 10 mol%, Cd starts to occupy Ca1 sites after filling one Ca2 site in the Ca2 hexagon. Thus, 10 mol% is a limited Cd content for occupying Ca2 sites only, which is also consistent with theoretical calculation results of excess energies that HAp with 10 mol% Cd has the lowest excess energy with Cd occupying Ca2 sites compared to mixed Ca1/Ca2 sites and Ca1 sites (Terra et al., 2010). Hence, we propose a conceptual model for Cd incorporation in HAp at different Cd contents (Figure 7). Cd ions first occupy hexagonal Ca2 positions since the Cd content is lower than 10 mol% (Figure 7a). As the Cd content increases to 10-20 mol%, Cd ions prefer to occupy the Ca1 site after one of the two Ca2 sites in each Ca2 hexagon is occupied (Figures 7b and 7c). Furthermore, it is deduced that Cd could occupy all Ca2 and Ca1 sites (Figure 7d) and eventually form the end member Cd-HAp \( \text{Ca}_6\text{Cd}_{10}(\text{PO}_4)_6(\text{OH})_2 \) (Hata et al., 1978; Lanfranco et al., 2003).
Figure 7. Representation of Cd incorporation into the HAp structure. (a) Cd in one Ca2 site (<10 mol%); (b) Cd in two Ca2 sites (10-20 mol%); (c) Cd in one Ca2 site and one Ca1 site (10-20 mol%); (d) Cd in two Ca2 sites and one Ca1 site (>20 mol%).

The effect of Cd preferentially at the Ca2 site may help us understand the change in lattice parameters with Cd incorporation. The decrease of $a$ and $c$ parameters has a very good linear relation with increasing Cd content at low Cd contents (<10 mol%), but shows a smaller decreasing rate at a Cd content of 16 mol% (Figure S3), which may result from Cd at Ca2 with a low Cd content and Cd at both Ca1/Ca2 sites with higher Cd contents. It has been reported that pure Cd2 substitution results in smaller lattice parameters $a$ and $c$ than pure Cd1 substitution in HAp (Tamm and Peld, 2006; Terra et al., 2010). This may explain our observed change in lattice parameters $a$ and $c$ where the decrease rate is reduced at higher Cd contents (Figure S3). With further increasing Cd content to form a complete Ca-Cd solid solution with mixed Cd2/Cd1 substitution, the change in lattice parameters becomes linear with Cd content in previous studies, in which the increased interval of Cd content is approximately 10 mol% (Lanfranco et al., 2003; Srinivasan et al., 2006; Terra et al., 2010).
The site preference of Cd in HAp also controls the dissolution process of Cd-HAp samples. Reported dissolution experiments show that HAp samples with various Cd contents exhibit different dissolution behaviors because of the preferred Ca sites for Cd (Zhu et al., 2016). Average solubility products ($K_{\text{sp}}$) changes largely from $10^{-57.65}$ (pure HAp) to $10^{-59.18}$ (HAp with 8 mol% Cd), but changes slowly at higher Cd contents (Zhu et al., 2016). This study provides a novel atomistic explanation that Cd only occupies the Ca2 site (<10 mol%) and alters kinetics for surface ions release (Terra et al., 2010). The preferred Ca2 site for Cd substitution could enhance Cd retention in the solid phase, as evidenced by sorption experiments, in which the sorption of Cd$^{2+}$ on HAp easily triggers coprecipitation of Cd-HAp (Srinivasan et al., 2006; Xu et al., 1994).

**IMPLICATIONS**

Cd is found to first occupy one Ca2 site at hexagonal Ca2 positions with Cd content lower than 10 mol%, and then begin to occupy the Ca1 site with increasing Cd content. The Cd incorporation only slightly changes the HAp long-range structure but increases structural disorder. As reported previously, Cd could diffuse into HAp during Cd sorption by HAp and form Cd-substituted HAp (Bailey et al., 2005; Xu et al., 1994). This study demonstrates that the incorporated Cd affects the HAp structure less than other metals (e.g., Zn$^{2+}$), revealing that the employment of HAp for Cd removal in contaminated water and soils should be effective. Natural soils and water only contain trace amounts of Cd (commonly <500 mg/kg (McLaughlin and Singh, 1999)), and the preferential occupancy of Ca2 via Cd under low Cd contents could contribute to long-term retention of Cd.

Metal-substitution in various minerals plays key roles in geochemical and environmental processes because substituted minerals commonly exhibit characteristics of both ions and modify surface reactivity. Cu-substituted HAp has been reported to enhance arsenate sorption compared...
to pure HAp (Liu et al., 2010). The increased surface area with Cd substitution suggests a potential improvement in the sorption of toxic elements (e.g., Pb, Zn, As, etc.) by Cd-substituted HAp. Additionally, the formation of solid-solutions has been widely employed to remove heavy metals from groundwater and soils and fix these heavy metals in solid phases for long-term remediation. Compared to surface adsorption, the Cd incorporation into the HAp structure implies that the Cd release from Cd-substituted HAp must break the HAp framework, suggesting that HAp could be a high-performance material for removing and storing Cd from contaminated environments.

SUPPLEMENTAL MATERIAL

Supplemental Material includes structural model of HAp, lattice parameters, Raman results, XANES spectra of P, Ca and Cd K-edge, fitting results of Ca $L_{2,3}$-edge TEY spectra, representation model for Cd incorporation, and fitting parameters of EXAFS spectra.

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REFERENCES


204(4963), 1050-1052.

energetics and geometry of sulfide, sulfite, and sulfate incorporation into apatite: The
thermodynamic basis for using this system as an oxybarometer. American Mineralogist,
102(8), 1646-1656.

Kobayashi, J. (1978) Pollution by cadmium and the itai-itai disease in Japan. In Toxicity of

nanocrystalline biocompatible single-phase Mn-doped A-type carbonated hydroxyapatite

Lanfranco, A.M., Schofield, P.F., Murphy, P.J., Hodson, M.E., Mosselmans, J.F.W., and
in soils: the application of Raman spectroscopy. Mineralogical Magazine, 67(6), 1299-
1316.

Alamos National Laboratory Report LAUR, 86-748.

Laurencin, D., Almora-Barrios, N., de Leeuw, N.H., Gervais, C., Bonhomme, C., Mauri, F.,
Chrzanowski, W., Knowles, J.C., Newport, R.J., and Wong, A. (2011) Magnesium
incorporation into hydroxyapatite. Biomaterials, 32(7), 1826-1837.


