Solubility of Calcium Phosphates

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Solubility is one of the most important properties of calcium phosphate salts. It is the solubility that determines the direction of many reactions that involve calcium phosphates such as dissolution, precipitation, hydrolysis, and phase transformation. Calcium phosphate solubility also plays a major role in biological processes that involve formation and resorption of hard tissues as well as pathological calcifications. This chapter will focus on concepts that would aid in gaining a better understanding of the solubility behavior of calcium phosphates, rather than provide a survey of the literature, which has been given elsewhere [Elliot, 1994]. Solubility is conventionally described as the amount of a solid that can dissolve into a unit volume of solution. For calcium phosphates, this quantity often changes by several orders of magnitude with changes in the pH and concentrations of acids and bases, such as HCl and NaOH. Thus, on the surface, the solubility may appear to be a complex function of these solution parameters. However, a clearer picture of the solubility properties for calcium phosphates can be gained by understanding the basic principles governing the solid-solution equilibrium.

Gibbs' Components

The composition of a solution may be described in terms of the quantities of independent components defined in Gibbs' phase rule [Gibbs, 1876]. The components may be understood as the minimum number of compounds that are needed to form all of the phases that may be present in a system. In the simplest case, a solution that contains calcium and phosphate ions is
comprised of three such components, e.g., Ca(OH)$_2$-H$_3$PO$_4$-H$_2$O [Moreno et al., 1966]. Because the components in a given phase must be homogeneously distributed, the Ca(OH)$_2$ and H$_3$PO$_4$ components here refer to materials dissolved in water, which is also a component. The selection of components is quite arbitrary and is usually based on the ease of expressing the concentrations and chemical potentials of the components. For example, CaO-P$_2$O$_5$-H$_2$O is another set of components that have been used in many studies [Brown and Lehr, 1959; Brown, 1992]. While considerable freedom exists in choosing components, these components must be independent in that a combination of any of the components does not form another component.

It is important to distinguish between the concept of a ‘component’ and that of a ‘species’. The Ca(OH)$_2$ and H$_3$PO$_4$ species refer to the undisassociated Ca(OH)$_2$ and H$_3$PO$_4$ present in the solution. An acidic solution with a pH of approximately 4.4 can be prepared by combining 0.01 moles of the compound Ca(OH)$_2$, 0.02 moles of the compound H$_3$PO$_4$, and a sufficient amount of water to make 1 liter of solution. While the concentration of the Ca(OH)$_2$ component in the solution is 0.01 mol/l, the concentration of the Ca(OH)$_2$ species is negligible at this pH because the bulk of the solution calcium is in the form of free Ca$^{2+}$ ions and a small amount is in the form of ion pairs with phosphate. A similar analysis can be made of a basic solution containing a significant amount of the H$_3$PO$_4$ component, but a negligibly small amount of the H$_3$PO$_4$ species because in alkaline solutions the solution phosphate are present primarily in the forms of HPO$_4^{2-}$ and PO$_4^{3-}$ ions. It can be seen from the above example that the concentrations of the Ca(OH)$_2$ and H$_3$PO$_4$ components are the same as the total calcium concentration, [Ca], and total phosphate concentration, [P], respectively, of the solution. As a result, these terms are equivalent and can be used interchangeably. For practical purposes, [Ca], [P], and pH are the three most commonly used parameters for describing the solution composition because all three are directly measurable quantities. The reason for expressing the solution composition in terms of Gibbs' components instead of [Ca], [P] and pH in this chapter is because of the ease of defining the solid-solution equilibrium described next.

**Solubility – Theoretical Considerations**

The dissolution reaction of a calcium phosphate solid, such as hydroxypatite (OHAp), may be expressed in two equivalent ways in terms of the ionic species (eq. 1) and the components (eq. 2).
Ca₃(PO₄)₂(OH) (solid) ⇌ 5 Ca²⁺ + 3 PO₄³⁻ + OH⁻  
Ca₃(PO₄)₂(OH) (solid) ⇌ 5 Ca(OH)²⁺ + 3 H₃PO₄ - 9 H₂O.  

The terms on the right hand side of the equations refer to the species or components in the aqueous solution phase. In a saturated solution in which the solid and solution are in equilibrium, eq. 2 leads to the chemical potential expression,

\[ \mu^{\circ}_{\text{OHAp}} = 5 \mu^{\circ}_{\text{Ca(OH)}_2} + 3 \mu^{\circ}_{\text{H}_3\text{PO}_4} - 9 \mu^{\circ}_{\text{H}_2\text{O}}. \]  

where \( \mu^{\circ}_{\text{OHAp}} \) is the chemical potential of OHAp at a standard state and is constant at a given temperature and pressure. The terms on the right hand side of the equation are the chemical potentials of the components in the aqueous solution. These quantities, which would vary with the composition of the solution, may be further described by the equations,

\[ \mu_{\text{Ca(OH)}_2} = \mu^{\circ}_{\text{Ca(OH)}_2} + RT \ln (\text{Ca}^{2+})(\text{OH}^-)^2, \]  
\[ \mu_{\text{H}_3\text{PO}_4} = \mu^{\circ}_{\text{H}_3\text{PO}_4} + RT \ln (\text{H}^+)(\text{PO}_4^{3-}), \]  
\[ \mu_{\text{H}_2\text{O}} = \mu^{\circ}_{\text{H}_2\text{O}} + RT \ln (\text{H}^+)(\text{OH}^-), \]

where \( \mu^{\circ} \) is the chemical potential of the designated component at a standard state and quantities in the parentheses are the activities. Substituting eq. 4–6 into eq. 3 gives

\[ \mu^{\circ}_{\text{OHAp}} - (5 \mu^{\circ}_{\text{Ca(OH)}_2} + 3 \mu^{\circ}_{\text{H}_3\text{PO}_4} - 9 \mu^{\circ}_{\text{H}_2\text{O}}) = RT \ln (\text{Ca}^{2+})(\text{PO}_4^{3-})(\text{OH}^-) \]  

The left hand side of eq. 7, which consists only of constant terms, is known as the standard free energy of dissolution for OHAp, \( \Delta G^{\circ}_{\text{OHAp}} \), as expressed in eq. 8.

\[ \Delta G^{\circ}_{\text{OHAp}} = \mu^{\circ}_{\text{OHAp}} - (5 \mu^{\circ}_{\text{Ca(OH)}_2} + 3 \mu^{\circ}_{\text{H}_3\text{PO}_4} - 9 \mu^{\circ}_{\text{H}_2\text{O}}). \]  

It is seen that \( \Delta G^{\circ}_{\text{OHAp}} \) is the difference between the standard chemical potential of the solid, OHAp, and the sum of the standard chemical potentials of the components in the solution multiplied by their respective coefficients that appear in the equilibrium equation (eq. 2). The variable part of the right hand side of eq. 7, \( (\text{Ca}^{2+})(\text{PO}_4^{3-})(\text{OH}^-) \), is known as the ion activity product for OHAp or IAP(OHAp). It follows from eq. 7 that for any solution that is saturated with respect to OHAp, IAP(OHAp) is related only to \( \Delta G^{\circ}_{\text{OHAp}} \) and therefore is a constant. Thus, for saturated solutions,

\[ K_{sp}(\text{OHAp}) = \text{IAP(OHAp)} = (\text{Ca}^{2+})(\text{PO}_4^{3-})(\text{OH}^-). \]  

where \( K_{sp}(\text{OHAp}) \) is known as the solubility product constant for OHAp. The Ksp value can be calculated from solubility measurement data, a knowledge of the dissociation constants of phosphoric acid and calcium hydroxide.
the various ion-pair formation constants, and an appropriate model for calculating the activity coefficients for the various species involved [McDowell et al., 1977]. Ksp, a thermodynamic property of the solid, is probably the most fundamental way of defining the solubility properties of a calcium phosphate. Although the Ksp value does not directly reveal the amount of the solid that can dissolve under a particular solution condition, it can be used to calculate solubility isotherms in a phase diagram to provide complete information on the solubility as a function of pH and other solution parameters as described next. Table 1 lists the Ksp values of the various calcium phosphate compounds that have been determined by different investigators.

**Solubility Phase Diagrams**

Gibbs' phase rule [Gibbs, 1876] dictates that under a fixed temperature and pressure, a three-component system, such as Ca(OH)$_2$-H$_3$PO$_4$-H$_2$O, with a single phase, e.g., a solution, has two degrees of freedom. It follows that the composition of any solution in this system is defined by fixing the values of two composition parameters, i.e., pH and [Ca], pH and [P], or [Ca] and [P]. Figure 1 shows a surface known as the 'electro-neutrality' surface [Brown, 1973] in a three-dimensional space with the coordinates being log [Ca], log [P], and pH of the solutions. Of all the solution compositions represented by the three-dimensional phase diagram, only those compositions that fall on the electro-neutrality surface satisfy the electro-neutrality condition, i.e., the sum of the charges carried by the anions and cations in the solution equals to zero, as given by the equation,

$$\sum_i u_i C_i = 0$$  \hspace{1cm} (10)

where $u$ and $C$ are the charge and concentration, respectively, of species $i$. Because they are electrically neutral, these are the only solutions that can exist physically. Thus, this surface defines the compositions of all solutions in the system without giving regards to the degree of saturation with respect to any solid. Shown on the surface are constant pH and [P] lines (fig. 1). It is seen in this diagram that the [Ca] of a solution is fixed by selecting the values of the other two composition parameters, pH and [P].

The Ca(OH)$_2$-H$_3$PO$_4$-H$_2$O system with two phases (a solution and a solid) in equilibrium has a single degree of freedom, and the composition of the saturated solution is completely defined by fixing the value of any one composition parameter, e.g., pH, [Ca], or [P]. Thus a line, known as a solubility isotherm in the phase diagram defines the compositions of a series of solutions, all of which are saturated with respect to the same solid, e.g., OHAp, and for which eq. 7 and 9 apply. The solubility isotherm of a calcium phospho-
Table 1. Calcium (ortho) phosphate compounds and their solubility product constants

<table>
<thead>
<tr>
<th>Compound</th>
<th>Formula</th>
<th>Ca/P</th>
<th>$-\log (K_{sp})$ at 25°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monocalcium phosphate monohydrate</td>
<td>$\text{CaH}_2\text{PO}_4\cdot\text{H}_2\text{O}$</td>
<td>0.5</td>
<td>highly soluble</td>
</tr>
<tr>
<td>Monocalcium phosphate anhydrous</td>
<td>$\text{CaH}_2\text{PO}_4$</td>
<td>0.5</td>
<td>highly soluble</td>
</tr>
<tr>
<td>Dicalcium phosphate anhydrous</td>
<td>$\text{CaPiO}_4$</td>
<td>1.0</td>
<td>6.90 [McDowell et al., 1968]</td>
</tr>
<tr>
<td>Dicalcium phosphate dihydrate</td>
<td>$\text{CaPiO}_4\cdot2\text{H}_2\text{O}$</td>
<td>1.0</td>
<td>6.59 [Gregory et al., 1970]</td>
</tr>
<tr>
<td>Octacalcium phosphate</td>
<td>$\text{Ca}_8\text{H}_2\text{PO}_6\cdot5\text{H}_2\text{O}$</td>
<td>1.33</td>
<td>96.6 [Ting et al., 1988]</td>
</tr>
<tr>
<td>$\alpha$-tricalcium phosphate</td>
<td>$\alpha-\text{Ca}_3(\text{PO}_4)_2$</td>
<td>1.5</td>
<td>25.5 [Fowler and Kuroda, 1986]</td>
</tr>
<tr>
<td>$\beta$-tricalcium phosphate</td>
<td>$\beta-\text{Ca}_3(\text{PO}_4)_2$</td>
<td>1.5</td>
<td>28.9 [Gregory et al., 1974]</td>
</tr>
<tr>
<td>Hydroxyapatite</td>
<td>$\text{Ca}_5(\text{PO}_4)_3\text{OH}$</td>
<td>1.67</td>
<td>58.4 [McDowell et al., 1977]</td>
</tr>
<tr>
<td>Fluorapatite</td>
<td>$\text{Ca}_5(\text{PO}_4)_3\text{F}$</td>
<td>1.67</td>
<td>60.5 [Moreno et al., 1977]</td>
</tr>
<tr>
<td>Tetracalcium phosphate</td>
<td>$\text{Ca}_6(\text{PO}_4)_3\text{O}$</td>
<td>2.0</td>
<td>38.0 [Matsuya et al., 1996]</td>
</tr>
</tbody>
</table>

Phosphate salt can be determined experimentally from solubility data. Alternatively, experimentally obtained solubility data can be used to calculate the Ksp of the solid which is then used to calculate the solubility isotherm. A calculated isotherm is useful for estimating solution compositions over a wider range than that covered by experimentally measured compositions. Figure 2 is a stereo pair of solubility phase diagrams showing the calculated isotherms (25°C) of seven salts: dicalcium phosphate dihydrate (DCPD), dicalcium phosphate anhydrous (DCPA), octacalcium phosphate (OCP), $\alpha$-tricalcium phosphate ($\alpha$-TCP), $\beta$-tricalcium phosphate ($\beta$-TCP), OHAp and tetracalcium phosphate (TTCP). Isotherms were calculated with the use of commercially available software (Chemist, Micromath, Salt Lake City, Utah, USA). Although the electroneutrality surface is not shown in figure 2, all isotherms do lie on this surface because all solutions must satisfy the electroneutrality requirement. Figures 3a–c show the phase diagram projected in two-dimensional spaces as viewed along the log [P], log [Ca], and pH axes, respectively. It can be seen in figure 3a that the isotherms have negative slopes in the neutral and acidic regions, i.e., pH below about 7, of the phase diagrams. This reflects the fact that all calcium phosphate compounds are more soluble as the pH decreases. The slope of the isotherm is an indication of how rapidly the solubility of the salt increases with decreasing pH. Since, for a given drop in pH, the solubility of a basic salt would increase more than would an acidic salt, the slope of the isotherm is related to the alkalinity of the salt. Consequently, the more acidic salts, DCPD and DCPA, have smaller negative slopes than do the more basic salts, TTCP, OHAp and the two TCPs.

In the alkaline regions of the phase diagram, the [Ca] increases with increasing pH (fig. 3a). In contrast, with the exceptions of DCPA and DCPD,
the [P] decreases with increasing pH (fig. 3 b). The reasons for the different shapes of the log [P] vs. pH isotherms are also related to the basicity of the compound as has been described previously [Chow et al., 1991]. It may be concluded that the solubility behavior of a calcium phosphate salt is principally determined by two factors: the Ksp and the basicity of the compound.

The solubility phase diagrams shown in figures 2 and 3 are quite useful because they reveal the relative stability of the salts at various pHs. At a given pH, a salt whose isotherm lies below that of another salt is less soluble (more stable) than the other. Thus, it is readily seen from the phase diagrams that OHAp is the least soluble among all salts until the pH falls below approximately 4.2 where DCPA becomes the least soluble. Similarly, TTCP is the most soluble salt for pH below 8.5; above that DCPD is the most soluble. Many phase transformation reactions reported in the literature can be understood through the use of these phase diagrams. For example, an acidic (pH 2.1) solution saturated with respect to DCPD was used as a pretreatment in a topical fluoridation procedure [Chow and Brown, 1975]. When the solution was applied to tooth enamel, the OHAp in enamel would dissolve, making the solution supersaturated with respect to DCPD, and DCPD would precipitate. At the same time, the pH of the solution would
increase from the initial value of 2.1 to a higher value, e.g., 3.5. The increase in pH is a result of dissolution of a more basic salt, OHAp, followed by precipitation of a more acidic salt, DCPD. Because the [Ca] and [P] are lower in the pH 3.5 solution than those in the pH 2.1 solution (fig. 3a, b), one would expect that this treatment should produce a net increase in mineral content in the enamel surface.

**Multicomponent Systems**

The phase diagrams shown in figures 2 and 3 apply only to the ternary system, Ca(OH)₂-H₃PO₄-H₂O. This means that the compositions described in these phase diagrams can be obtained by equilibrating a calcium phosphate salt in water or aqueous solutions containing H₃PO₄ and Ca(OH)₂ only and not in solutions that contain components other than those in the ternary system, e.g., HCl or NaOH. However, diagrams similar to figures 2 and 3 can be constructed for a quaternary system in which the quantity of
Fig. 3. The solubility phase diagrams shown in figure 2 projected on log [Ca] vs. pH plane (a); log [P] vs. pH plane (b), and log [Ca] vs. log [P] plane (c).
the fourth component is held constant. Figure 4 is a stereo pair of solubility phase diagrams showing solubility isotherms for OHAp in the four-component system, Ca(OH)$_2$-H$_3$PO$_4$-U($\pm$)-H$_2$O, where U($+$) is NaOH or U($-$) is HCl. Each OHAp isotherm is for a fixed concentration of U($+$) or U($-$) at 0 mol, 10$^{-4}$, 10$^{-3}$, 10$^{-2}$ or 10$^{-1}$ mol/l. Figure 5a-c show the same diagram projected in a two-dimensional space viewed along the log [P], log [Ca], and pH axes, respectively. It can be seen in figure 5c that the primary effects of NaOH or HCl, which does not form significant amounts of stable ion-pairs or insoluble salts with calcium or phosphate ions, are to shift the loci of the isotherms. The [P] of all points on the isotherms for the NaOH-containing systems are increased from the corresponding values in the ternary system, simply to balance the positive charges carried by the Na$^+$ ions. Similarly, the [Ca] are higher in proportion to the HCl content of the solutions in order to balance the negative charges of the Cl$^-$ ions. Additionally, the increase in [Ca] causes a reduction in the [P] needed to satisfy the Ksp such that the isotherms plotted in the form of log [P] vs. pH are significantly shifted toward lower P concentrations (fig. 4b). Diagrams similar to figures 4 and 5 may be constructed for other calcium phosphate salts. In the cases where an acid is partially dissociated or forms stable complexes with calcium or phosphate ions, knowledge of the acid or complex dissociation constants is required to produce the phase diagram.

**Chemical Potential Diagrams**

Figures 2-5 show the relationships of directly measured quantities, [Ca], [P], and pH, of solutions that are saturated with respect to the various solids. Another type of solubility phase diagram, known as a potential diagram, provides a different way to understanding the solubility properties of calcium phosphates. Rearrangement of eq. 3, which is valid for all solutions saturated with OHAp, yields the following equation.

\[
\mu_{\text{Ca(OH)}_2} = -3.5\mu_{\text{H}_2\text{PO}_4} + 1/5 (\mu_{\text{OHAp}} + 9\mu_{\text{H}_2\text{O}}).
\] (11)

For dilute solutions, $\mu_{\text{H}_2\text{O}}$ can be considered constant and the second term on the right hand side of the equation becomes a constant. It follows that for all solutions saturated with respect to OHAp, there exists a linear relationship between $\mu_{\text{Ca(OH)}_2}$ and $\mu_{\text{H}_2\text{PO}_4}$. The slope of this straight-line relationship, $-3.5$, is equal to the negative reciprocal of the molar Ca/P ratio of the solid. When eq. 4-6 are substituted into eq. 11, one obtains

\[
\ln (\text{Ca}^{2+})(\text{OH})^2 = -3.5 \ln (\text{H}^+)(\text{PO}_4^{3-}) + K.
\] (12)
Fig. 4. A stereo pair of solubility phase diagrams for the quaternary system, Ca(OH)$_2$-H$_3$PO$_4$-U(±)-H$_2$O, at 25°C showing OHAp isotherms at fixed pU(±) values in a three-dimensional space.

where $K$ is a constant comprising of the standard chemical potentials of OHAp and the components Ca(OH)$_2$ and H$_3$PO$_4$, and the chemical potential of H$_2$O. This shows that the logarithms of the activities of the two components, Ca(OH)$_2$ and H$_3$PO$_4$, are also linearly related. Similar linear relationships can be derived for other calcium phosphates, and figure 6 shows the straight-line relationships for the seven calcium phosphate salts whose isotherms are given in figures 2 and 3. It can be shown that in this diagram solutions located to the right of the straight-line are under-saturated and those to the left of the straight-line are supersaturated with respect to the solid.

It should be noted that eq. 11 and 12 hold true for all solutions that are saturated with OHAp regardless of whether or not any other components, such as HCl or NaOH, are also present. As a result, the potential diagram
Fig. 5. The solubility phase diagrams shown in figure 4 projected on log [Ca] vs. pH plane (a); log [P] vs. pH plane (b), and log [Ca] vs. log [P] plane (c).
(fig. 6) is quite useful in multicomponent systems because a single line represents all the solubility isotherms with different \(U(\pm)\) values for OHAp shown in figure 4. Because the activities, \((Ca^{2+})(OH)^{-}\) and \((H^+)(PO_4^{3-})\), of a solution can be calculated from directly measurable quantities, i.e., pH, [Ca], [P], [Na], and [Cl], a solution can be represented as a point in the potential diagram, and the degrees of saturation with respect to the various solids will be revealed. The potential diagrams have proven useful in a number of studies in attempting to identify the phase(s) with which the solution may be in equilibrium at different times of the reaction process. The potential diagram is especially useful for studies dealing with complex biological samples. For example, based on potential plots of solubility data, MacGregor and Brown [1965] concluded that equilibration of child and calf bone mineral with serum followed OCP solubility, whereas adult bone mineral followed apatite solubility.

**Solubility of Solid Solutions**

An apatitic mineral that contains both F\(^-\) and OH\(^-\) ions may be considered as a solid solution of FAp and OHAp with the general formula \(Ca_x(PO_4)_3(OH)_{1-x}F_x\), where \(0 \leq x \leq 1\). Other apatitic compositions resulting from similar substitutions may also be considered solid solutions, for example, substitution of \(CO_3^{2-}\) for \(PO_4^{3-}\) with a general formula of \(Ca_{10-x-y}(PO_4)_{6-x}(CO_3)_x(OH)_{2-x+y}\) and \(0 \leq x \leq 2\) and \(0 \leq y \leq 0.5\) x [Labarthe et al., 1973]. The solubility properties of these solid solutions are more complex because as the solid-liquid equilibrium is being approached, a change in the solid composition (change in the \(x\) or \(u\) value) may occur on the surface of the crystalline particles such that the surface phase has the least soluble (most stable) composition for the particular aqueous solution composition [Driessens, 1979]. Consequently, the solid phase that would reach true equilibrium with the aqueous solution may have a different \(x\) value from that of the bulk solid. Despite the potential difficulties in obtaining reliable \(K_{sp}(x)\) values as a function of \(x\), Driessens [1982] analyzed the solubility data reported in the literature [Narasaraju, 1974; Moreno et al., 1977; Verbeeck et al., 1980] and concluded that the presence of F\(^-\) ions in the apatitic crystal structure reduces the solubility (in terms of the amount soluble) of OHAp considerably, especially at low pH; a reduction of solubility of at least 80% can be expected at pH 4 for a \(Ca_5(PO_4)_3(OH)_{1-x}F_x\) solid solution with an \(x\) value of 0.1.

In an attempt to understand the solubility behavior of the solid solutions as a function of the aqueous solution composition, Chow and Marko-
Fig. 6. Potential phase diagram at 25°C showing solubility isotherms of various calcium phosphate salts.

Vic [1998] conducted a theoretical analysis to determine which factors are the major determinants of the x value of the least soluble (most stable) solid for a particular aqueous solution composition. They concluded that the stability of the solid solutions depends entirely on how $K_{sp}(x)$ varies with x. It was shown that OHAp is less soluble (more stable) than fluorapatite (FAp) and any of the solid solutions in aqueous solutions that have relatively high pH and low $[F]$, while FAp is less soluble than OHAp and any of the solid solutions in aqueous solutions that have relatively low pH and high $[F]$. The solubility properties of the solids in aqueous solutions between these two extremes would depend on how $K_{sp}(x)$ varies with x. When $K_{sp}(x)$ is a linear function of x, all of the solid solutions are more soluble than OHAp or FAp except in one series of aqueous solutions in which OHAp and FAp as well as all of the solid solutions are equally soluble. Since the solid solutions can exist only under this extremely confined condition, they play no significant roles in the dissolution behaviors of OHAp and FAp. In the case where the $K_{sp}(x)$ value falls below that predicted by the linear function, there will be a region in the aqueous compositions where a solid solution with a specific x value is less soluble than OHAp, FAp, or other solid solutions. In these cases, there are no stable aqueous solutions that are simultaneously saturated with respect to both OHAp and FAp, the two end members of the so-
lid solution series, but an aqueous solution can be simultaneously saturated with respect to two adjacent members of the series. A solid solution with a smaller \( x \) value tends to be more stable in solutions with higher \( \text{pH} \) and lower \([\text{F}]\); those with a larger \( x \) values are more stable in solutions with lower \( \text{pH} \) and higher \([\text{F}]\). While it is possible to analyze the solubility properties of simple solid solutions, such as \( \text{Ca}_x(\text{PO}_4)_y(\text{OH})_{1-y}\) \( X \), in a rigorous way, most biologically and geologically formed apatitic minerals contain a large number of different impurity ions. Their solubility behavior has been studied with a more empirical approach as described below.

**Variable Solubility of Biominerals**

A solid with a fixed composition and crystallinity has a well-defined standard chemical potential (\( \mu^0 \)). A constant Ksp value would be expected from such a solid based on theoretical considerations, i.e., eq. 3-9, given earlier. Several calcium phosphate salts, such as DCPA [McDowell et al., 1971] and DCPD [Gregory, 1968], appear to fall into this category, and constant Ksp values have been obtained from solubility measurements conducted under a wide range of experimental conditions. In contrast, OHAp, OCP, and \( \beta\)-TCP, are able to include significant amounts of structurally incorporated foreign ions [LeGeros, 1991] such as \( \text{H}^+ \), \( \text{Na}^+ \), \( \text{Mg}^{2+} \), \( \text{Cl}^- \), \( \text{F}^- \), and \( \text{CO}_3^{2-} \), and to tolerate structural imperfections. For these solids, the \( \mu^0 \) would be expected to have a range of values, and variations in the Ksp value are inevitable. In some cases, the impurity content can vary continuously, making it difficult to determine the Ksp experimentally, as in the case with solid solutions described earlier.

Solubility properties of human dental enamel and bone mineral have been a subject of great interest because of their roles in hard tissue formation and disease processes. Dissolution properties of carbonate-containing apatitic minerals have also been investigated in numerous studies as synthetic analogues of biological apatites. In earlier studies [Patel and Brown, 1975], OHAp was assumed to be the phase that would be in equilibrium with the solution, and the solubility of the mineral was expressed in terms of IAP(OHAp), i.e., with the use of eq. 9. In later studies, a formula that included some of the impurity ions, such as \( \text{Ca}_{5-x-y}(\text{HPO}_4)_x(\text{PO}_4)_{3-x-y}(\text{CO}_3)_y(\text{OH})_{1-x-y} \) was used [Moreno and Aoba, 1990] as the entity that governed the equilibrium. Several studies also included different levels of \( \text{CO}_2 \) partial pressure to help establish equilibrium between the carbonate in the solid and solution phases [Moreno and Aoba, 1990; Larsen et al., 1997]. Regardless of the IAP formula or the experimental conditions used, many
studies reported that the incorporated foreign ions, e.g., Na\(^+\), Mg\(^{2+}\), Cl\(^-\) and CO\(_3\)^{2-}\), were preferentially liberated [Larsen et al., 1997], and nearly all of the studies found that the experimentally determined Ksp varied significantly with the experimental conditions. While there is a large body of literature demonstrating the effects of structural and compositional variations in biologically formed minerals on Ksp, a clear understanding of the mechanisms is lacking.

More recently, a new approach was used [Fox et al., 1995] to gain a better understanding of the variable solubility phenomenon of synthetic carbonated apatites, biological apatites, and perhaps apatitic mineral in general. The model employs two new concepts to describe the solid-solution equilibrium:

1. Metastable equilibrium solubility (MES): The MES behavior occurs when a crystalline material dissolves relatively rapidly, leading to a solution composition such that no further dissolution occurs, even though the degree of saturation is significantly below that required for crystal growth. The investigators found that a given mineral sample does not exhibit a single MES value but a MES profile (a range of MES values).

2. Dissolution-governing surface complex: The surface complex is visualized as an entity forming at the crystal surface in contact with the ions in solution, and it determines the functional form of the dissolution driving force. The formula of the complex, which is often different from

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Fig. 7. Schematic drawing of three MES profiles.
the composition of the bulk mineral, can be experimentally determined from solubility data.

To help understand the concept of MES distribution, figure 7 shows 3 hypothetical MES profiles for minerals with a surface complex of Ca$_{5}$P$_{6}$O$_{24}$OH and the metastable equilibrium solubility product defined as MES K$_{sp}$ = (Ca$^{2+}$)$_{5}$(PO$_{4}^{3-}$)$_{3}$(OH$^{-}$). A MES profile is the MES K$_{sp}$ that the mineral sample exhibits as a function of the fraction of the mineral that had been dissolved. Profile A has a lower mean MES pK$_{sp}$ value than does profile B, indicating that mineral A is on average more soluble than mineral B. Profile A also has a wider MES distribution, indicating that its solubility covers a wider range. When the MES distribution converges to a step function (profile C), it exhibits a single value, approaching the conventional solubility product constant.

A number of interesting findings have been reported from studies that used this approach. Carbonated apatite dissolution kinetics were found to be governed by an OHAp surface complex, and not a carbonate-containing complex [Hsu et al., 1994]. When the MES of a large number of carbonated apatite samples prepared at different temperatures and with different carbonate contents were examined, the mean MES was not directly related to the carbonate content, but rather to the crystallinity of the mineral as measured by the (002) x-ray diffraction peak width. When crystallinity was taken into account, the carbonate content did not have any further effects on MES [Baig et al., 1996]. With the use of the Rietveld method of whole x-ray diffraction pattern structure refinement, the effects of carbonate on two different crystallinity parameters, crystal size and microstrain were determined [Baig et al., 1999]. The results showed that it was microstrain, rather than crystal size, that predominantly determined the MES of carbonated apatites and dental enamel. These studies have advanced significantly our understanding of the mechanisms through which the compositional and crystal structural modifications brought about by the impurity ions affect the dissolution behavior of apatites. Further studies will be able to determine whether the MES model is applicable over a wide range of aqueous compositions that include the full range of impurity ions, e.g., Na$^{+}$, Mg$^{2+}$, Cl$^{-}$, F$^{-}$, and CO$_{2}^{-}$, that are present in the minerals.

**Concluding Remarks**

The discussions of calcium phosphate solubility behavior given in this chapter are focused on understanding the basic principles that govern the solid-solution equilibrium and on the use of solubility phase diagrams to de-
scribe the solubility over a wide range of concentrations and in the presence of additional components. In reality, the dissolution process is often made more complex by additional concomitant processes such as the solution-solid surface equilibriums described by Tung and Skrtic [2001, this volume]. A clear understanding of the solubility behavior offers a good starting point for gaining insight into more complex processes such as hydrolysis [Tung et al., 1985], phase transformation [Radin and Ducheyne, 1993], incongruent dissolution [Kaufman and Kleinberg, 1979], calcium phosphate cement setting reactions [Chow et al., 1991] and demineralization of enamel in the caries process [Vogel et al., 1988].

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