Bull. Chem. Soc. Jpn., 60, 1141—1143 (1987)

A Structural Model for Octacalcium Phosphate-Succinate Double Salt

Mathai MATHEW* and Walter Eric BROWN
Paffenbarger Research Center, American Dental Association Health Foundation,
National Bureau of Standards, Gaithersburg, MD 20899, U.S.A.
(Received January 20, 1986)

A new structural model for octacalcium hydrogenpentakis(phosphate) succinate pentahydrate, $Ca_8H(PO_4)_5(C_2H_4\cdot(COO)_2)\cdot 5H_2O$, a reaction product of octacalcium dihydrogenhexakis(phosphate) pentahydrate, $Ca_8H_2(PO_4)_6\cdot 5H_2O$, OCP, and succinate ions, is proposed on the basis of similarities in the unit cell dimensions and structures of OCP and calcium succinate trihydrate. This model can be used to develop information on the mode of incorporation of dicarboxylate ions into OCP and hydroxyapatite and its possible effects on biological mineralization processes.

Monma et al.[1,2] have recently made the discovery that saturated aliphatic dicarboxylic acids, $HOOC-(CH_2)_n-COOH$ with $n=1$ to 6, form a series of double salts with octacalcium dihydrogenhexakis(phosphate) pentahydrate, $Ca_8H_2(PO_4)_6\cdot 5H_2O$; generally referred to as octacalcium phosphate (OCP). They proposed that the double salts are formed by substitution of an HPO_4^{2-} group in OCP by a dicarboxylate ion, with the general formula, $Ca_8(HPO_4)_{2-z}(PO_4)_4\cdot(C_nH_{2n}C_2O_4)_z\cdot mH_2O$, and gave a possible structural model. We propose here a different model for the structure of one of these double salts, octacalcium hydrogenpentakis(phosphate) succinate pentahydrate, $Ca_8H(PO_4)_5(C_2H_4\cdot(COO)_2)\cdot 5H_2O$, based on the observation that the non-primitive, B-centered cell of calcium succinate trihydrate has *b* and *c* dimensions and the angle γ which are very similar to those of OCP[3] and hydroxyapatite (OHAp), $Ca_5(PO_4)_3(OH)$ (Table 1). It was the similarities between the same dimensions of OCP and OHAp that revealed the structural relationship between these two salts which so profoundly affects their physical and chemical properties. At this time, very little is known about the properties of the double salts, but if they form as biominerals, they probably will prove to affect properties such as crystal growth and hydrolysis, morphology, Ca/P ratio and impurity content of hydrolysates.

The structural model for the OCP-dicarboxylate complexes proposed by Monma[2] is based on the structure of OCP[3] and the structures of the corresponding dicarboxylic acids. The model was conceived on the assumption that the [Ca-HPO_4-Ca] pillar in the hydrated layer of OCP (Fig. 1) is substituted by a [Ca-dicarboxylate-Ca] pillar. The [Ca-HPO_4-Ca] pillars implicated in their model are Ca(3)-P(5)′HPO_4-Ca(4)′ and Ca(4)-P(5)HPO_4-Ca(3)′ (Fig. 1). Based on the structure of OCP, P(5)HPO_4 would be the most likely candidate to be involved in the replacement. Since the projection of the Ca(3)-dicarboxylate-Ca(4) pillar onto the *a*-*b* plane is nearly parallel to the a axis, the increase in d_{100} of OCP-dicarboxylate would be proportional to the length of the dicarboxylate ion.

The model proposed by Monma has several drawbacks. The plane of the COO^- group is approximately parallel to the c-axis and the model requires two dicarboxylate ions to be nearly superimposed along the relatively short c-axis (6.88 Å). Furthermore, when the whole unit cell is taken into account, particularly in the *a*-*b* plane (001), it becomes obvious from their model that there would be a relatively large volume of empty space in the center of the cell. The increase of d_{100} (e.g. from 18.7 Å in OCP to 21.4 Å in OCP-succinate) would make the apparent volume of this empty space even larger. It is unlikely that this space could be occupied by water molecules or other ions because its major boundaries would be the hydrophobic part (methylene groups) of the dicarboxylate ions. This would be particularly true for the higher members of the series. However, this model may be possible in the case of dicarboxylic acids with additional functional groups (OH, NH_2, COOH) which are more compatible with ions and water molecules.

A New Model. Our model is based on the structure of calcium succinate trihydrate. The structure is reported[4] in the space group $P\bar{1}$ with $a=7.937$, $b=9.450$, $c=6.688$ Å, $\alpha=91.47$, $\beta=111.80$, and $\gamma=71.60°$. The transformation matrix $(2\ 0\ \bar{1}/0\ \bar{1}\ 0/0\ 0\ \bar{1})$ converts this primitive cell to a B-centered cell with the dimensions listed in Table 1. The striking similarity of this cell to those of OCP and OHAp is immediately obvious. The cell dimensions *b* and *c* and all cell angles of the succinate and OCP are nearly identical.

Table 1. Comparison of Cell Dimensions in OCP, OHAp, and Calcium Succinate Trihydrate

	OCP	OHAp	Ca succinate trihydrate
a/Å	19.692	9.432	14.759
b/Å	9.523	9.432	9.450
c/Å	6.835	6.881	6.688
α/°	90.15	90.0	91.47
β/°	92.54	90.0	93.08
γ/°	108.65	120.0	109.14
Space group	$P\bar{1}$	$P6_3/m$	$B\bar{1}$

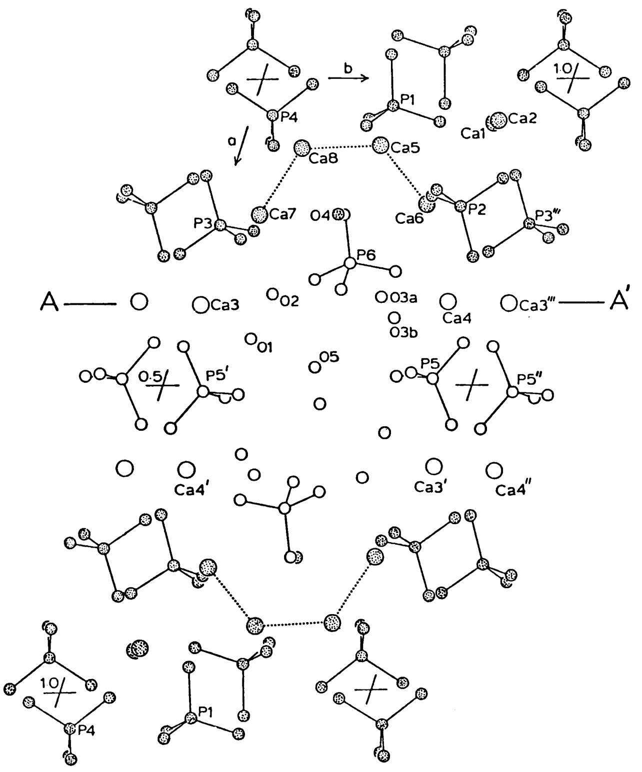

Fig. 1. Structure of OCP projected down the c* axis. The shaded portions correspond to the apatitic layer and the nonshaded atoms correspond to the hydrated layer. Atoms in the asymmetric unit are labelled. Symmetry codes for related atoms are ′ for (1−*x*, 1−*y*, −*z*), ″ for (1−*x*, 2−*y*, −*z*) and ‴ for (*x*, 1+*y*, *z*).

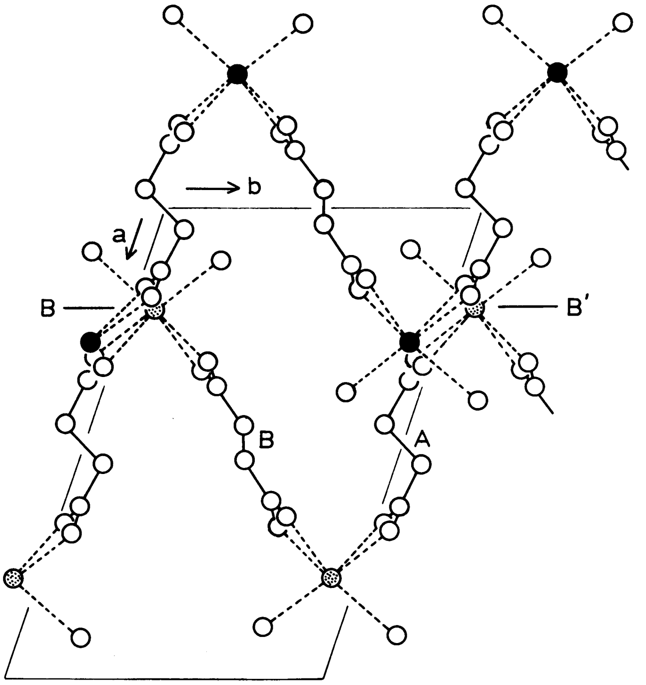

Fig. 2. Structure of calcium succinate trihydrate projected down the c* axis. The filled circles represent Ca atoms at $z=1/2$ and the shaded circles the Ca atoms at $z=0$.

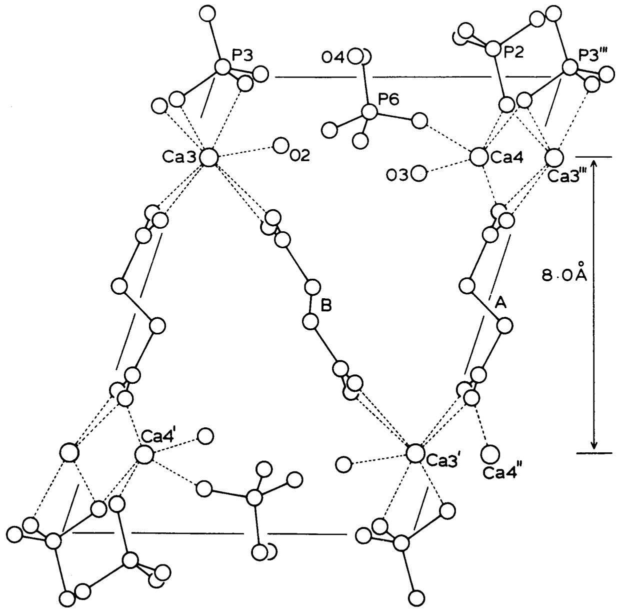

Fig. 3. The proposed model of OCP–succinate, viewed down the c* axis. Only the central portion of the OCP cell ($a=1/4$—$3/4$) showing the incorporated succinate ions is illustrated.

Comparison of the structures of OCP (Fig. 1) and calcium succinate trihydrate (Fig. 2) reveals some important structural similarities. The unit cell dimensions in the (100) planes of the two compounds are nearly the same. The relative positions of the Ca ions in a section of this plane through Ca(3)–Ca(3)‴ in OCP (A–A′ in Fig. 1) are nearly identical to those of a corresponding section, B–B′, in calcium succinate trihydrate (Fig. 2). This implies that epitaxial growth of calcium succinate on the (100) plane of OCP is possible, and that on a sub-unit cell level the OCP structure at A–A′ can be joined to the calcium succinate structure at B–B′ (Fig. 3). A feature of the structure of calcium succinate is that the succinate ions reside on crystallographic centers of symmetry and link pairs of equivalent Ca ions at the same height along c axis in a zigzag way. The succinate ions linking the Ca ions at $z=1/2$ are not on top of those linking the Ca ions at $z=0$, but related by $1/2a+1/2c$ (B-centering). This is to be expected on steric grounds.

The model we propose for the OCP–succinate complex takes into account the structural features of both OCP and calcium succinate trihydrate. Based on the structure of the calcium succinate, it is obvious that the succinate ion, which lies on a center of symmetry, can link only pairs of one type of Ca ion (either Ca(3) or Ca(4)) in the hydrated layer of OCP. On the basis of bond length calculations, Ca(3) appears to be a more probable candidate than Ca(4) for linking succinate ions in the OCP–succinate complex. It is interesting to note that the position of Ca(3) in OCP corresponds very closely to that of a column calcium in OHAp whereas the Ca(4) position in OCP is shifted by about 1.9 Å along the b axis. Although the Ca(4)–Ca(4)″ (Fig. 1) linkage through a succinate ion is possible, an increase in d_{100} due to the incorporation of this succinate would make the Ca(4)···Ca(4)′ distance considerably longer than that which can be linked by the succinate ion unless there is a corresponding shift of Ca(4) along the b axis.

Our proposed structure contains two types of succinate ions. One succinate ion (A) links Ca(3)‴ and Ca(3)′ of OCP (Fig. 1) primarily along the a axis, thus causing a corresponding increase in d_{100}. In effect, this succinate ion replaces two HPO_4^{2-} ions of OCP. The second succinate ion (B) links Ca(3) and Ca(3)′, without affecting the d_{100} spacing. The succinate ion B is far removed from the HPO_4 ion sites of OCP and fills the void that would otherwise exist in the center of the unit cell.

The proposed model is illustrated in Fig. 3. Most of the structural features of OCP remain intact. The water molecules O(2), O(3), and O(4) in OCP would retain their respective positions in the complex; only O(1) and O(5) need to be relocated if the total amount of water content is to remain the same as in OCP as indicated by the molecular formula proposed by Monma.2) The proposed structural model implies that at least one of these two water molecules is likely to be coordinated to Ca(4).

The [Ca–succinate–Ca] pillar length down c^* in calcium succinate of 8.0 Å (Fig. 2) would make the d_{100} of the OCP–succinate complex 21.6 Å which is in reasonably good agreement with the experimental value2) of 21.4 Å. Since the dicarboxylate ions are capable of adopting different conformations, the difference may not be significant.

In OCP, both Ca(3) and Ca(4) are coordinated to seven O atoms. In our proposed structure of OCP–succinate, four of these bonds remain intact. In the case of Ca(3), it loses three O neighbors (two from $P(5)HPO_4$ and one from water molecule O(1)), but gains four O from carboxylato groups. Thus the coordination of Ca(3) is 8. However, Ca(4) loses three O neighbors, all from $P(5)HPO_4$ groups, but appears to gain only one O from carboxylato group in succinate A. In calcium succinate, the Ca ion corresponding to Ca(4) is linked to two O atoms of the type A succinate ion, one above and one below the plane of Ca(4). The same configuration of Ca(4) may be achieved in OCP–succinate also, with minor shifts in the positions of Ca(4) and/or with succinate A.

Discussion

When it was first observed that OCP and OHAp had very similar unit-cell parameters *b*, *c*, and angle *γ*, it was proposed that the two compounds contain a structurally similar layer. This was subsequently established by the determination of the structure of OCP. Nearly identical unit-cell parameters, *b*, *c*, and angle *γ*, are present in the OCP–succinate salt and in calcium succinate trihydrate. Although this could be a coincidence, it is more likely that the OCP–succinate and the calcium succinate trihydrate contain a common layer which is compatible with the OCP structure. This hypothesis is substantiated by the presence of Ca(3) and Ca(4) in OCP which occupy positions similar to those in calcium succinate trihydrate. Furthermore, when the d_{100} of OCP, 18.7 Å, is increased to that of the OCP-succinate complex, 21.6 Å, the Ca(3)‴–Ca(3)′ and Ca(3)–Ca(3)′ distances (Fig. 1) become such that they can accept succinate bridge coordination similar to those found in calcium succinate trihydrate. We conclude, therefore, that the model proposed in Fig. 3 for OCP–succinate structure is probably a good approximation and that it can be used (i) to visualize the structure of the OCP–succinate complex and (ii) to develop mechanisms for the hydrolysis and growth of OCP–succinate crystals.

Calcium malonate has two crystalline forms, both dihydrates, whose structures are known.5,6) However, we were not able to transform their unit cells to have *b*, *c*, and *γ* values compatible with OCP. Examinations of the structures did not reveal compatibilities such as those found in calcium succinate trihydrate. This does not, of course, preclude formation of an OCP–malonate complex detected by Monma,2) but it suggests that despite the near constancy of the increase in d_{100} with increase in length of the aliphatic carbon chain, there may be substantial differences among the structures of the double salts. Another indication of this is the inability of the dicarboxylate ions with an odd number of carbon atoms to reside on a center of symmetry.

This investigation was supported in part by Grant DE 05030 to the American Dental Association Health Foundation by the National Institutes of Health-National Institute of Dental Research and is part of the Dental Research Program conducted by the National Bureau of Standards in cooperation with the American Dental Association Health Foundation.

References

1) H. Monma and M. Goto, *Bull. Chem. Soc. Jpn.*, **56**, 3843 (1983).

2) H. Monma, *Bull. Chem. Soc. Jpn.*, **57**, 599 (1984).

3) W. E. Brown, *Nature (London)*, **196**, 1048 (1962).

4) A. Karipides and A. T. Reed, *Acta Crystallogr., Sect. B*, **36**, 1377 (1980).

5) B. Briggman and A. Oskarsson, *Acta Crystallogr., Sect. B*, **33**, 1900 (1977).

6) J. Albertsson, A. Oskarsson, and C. Svensson, *Acta Crystallogr., Sect. B*, **34**, 2737 (1978).