EMMA INSTITUTE OF TECHNOLOGY

PROJECT ADMINISTRATION DATA SHEET

Project No.  G-41-635 (19th year)  DATE  6/18/82

Project Director:  Dr. R.A. Young  School/  Physics

Sponsor:  NIH: National Institute of Dental Research

Type Agreement:  Grant No. 5R01DE01912-19

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Title:  Tooth Enamel Apatite at the Atomic Level

ADMINISTRATIVE DATA

OCA Contact  William F. Brown  x4820

1) Sponsor Technical Contact:

Paul D. Fraizer, D.D.S., Ph.D.

Chief, Soft Tissue Stomatolgy

& Nutrition Program Branch

(301) 496-7807

Defense Priority Rating:  N/A

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RESTRICTIONS

Attached  N/A  Supplemental Information Sheet for Additional Requirements.

Travel:  Foreign travel must have prior approval — Contact OCA in each case. Domestic travel requires sponsor approval where total will exceed greater of $500 or 125% of approved proposal budget category

Equipment:  Title vests with GIT

COMMENTS:

Dr. Young is transferring his project B-447-007/EML to Physics effective July 1, 1982. The project will be completely transferred as soon after July 1 as the books can be closed on the EES portion.

WORDS TO:

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Date April 5, 1984

Project No. G-41-635

Includes Subproject No.(s)

Project Director(s) Dr. R. A. Young

Sponsor NIH; National Institute of Dental Research

Title Tooth Enamel Apatite at the Atomic Level

Effective Completion Date: 4/30/83 (Performance) 7/31/83 (Reports)

Grant/Contract Closeout Actions Remaining:

- None

- Final Invoice or Final Fiscal Report

- Closing Documents

- Final Report of Inventions

- Govt. Property Inventory & Related Certificate

- Classified Material Certificate

- Other

Continues Project No. G-41-635

Continued by Project No. G-41-643

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THE LONG TERM GOAL IS THE ELUCIDATION, AT THE ATOMIC LEVEL, OF PHENOMENA AND MECHANISMS IMPORTANT TO THE UNDERSTANDING AND ULTIMATE MODIFICATION OF THE BIOLOGICAL OCCURRENCE, FUNCTION AND DYSFUNCTION OF THE APATITIC PORTION OF DENTAL HARD TISSUE. VARIOUS ATOMIC/IONIC SPECIES PRESENT IN HUMAN TOOTH ENAMEL (TE) ARE BEING STUDIED (1) FOR THEIR PRECISE STRUCTURAL LOCATIONS AND ROLES AND (2) FOR THE ATOMIC-SCALE MECHANISMS BY WHICH THEY AFFECT DIFFUSION, ACID DISSOLUTION, AND THE RESPONSE OF TE TO VARIOUS TREATMENTS AND ENVIRONMENTS. THE STRUCTURAL MODEL FOR THE CRYSTALLINE PORTION OF TE IS CONSTANTLY BEING IMPROVED TOWARD REALISM AS THE LOCATIONS AND ROLES ARE FURTHER CLARIFIED FOR $\text{CO}_3^-$, $\text{HPO}_4^-$, $\text{H}_2\text{O}$, $\text{Na}^+$, $\text{Mg}^{2+}$, $\text{Sr}^{2+}$, $\text{Zn}^{2+}$, $\text{Pb}^{2+}$, VACANCIES, AND FOR $\text{Cl}^-$, $\text{F}^-$ AND OXYGEN SUBSTITUTING FOR THEM. PRINCIPAL EXPERIMENTAL METHODS ARE X-RAY AND NEUTRON DIFFRACTION (ESPECIALLY RIETVELD ANALYSIS), I.R. SPECTROSCOPY, DEUTERIZABILITY, EXAFS, AND VARIOUS CHEMICAL PREPARATION AND ANALYSIS METHODS. STUDIES ARE CARRIED OUT BOTH DIRECTLY ON TE AND ON RELATED APATITE COMPOUNDS.
Privileged Communication

A4. COMPREHENSIVE PROGRESS REPORT

A4. b. Summary

Progress has been made in several areas, all of which relate either directly or through intermediate steps to the nature and properties of biological apatite (human tooth enamel, TE). Particular attention is given to the properties of TE and to hydroxyapatite (OHAp) and chlorapatite (ClAp) as being related simpler systems. Progress has been made toward developing atomic-level model descriptions of ways and consequences of differences between OHAp and real biological apatite (TE), which accommodates a rich variety of substitutions and defects, each of which contributes something to TE properties. Specific new results of interest include the following:

1) Deuterizability, in terms of kinetics and limitations of deuteration, has become an important and especially informative tool for studying phenomena related to OH (and H$_2$O) diffusion in apatites and TE.

2) The inhibiting effect of F on OH diffusion, first reported in 1969, has been quantified: In one set of deuteration experiments with synthetic OHAp, the OH ions adjacent to F ions (hydrogen bonded) were shown to be released for exchange with OD at only 70\% of the rate of those OH ions not associated with F. This effect may be at the basis of fluoride action.

3) The variability of pure synthetic hydroxyapatite preparations has been demonstrated, with deuterizability as a tool, to be a normal feature of OHAp preparations. The variation is now thought to be attributable to vacancies and disorder. They occur least in strongly heated preparations which then are monoclinic. The vacancies and disorder occur much more in unheated aqueous preparations, which are hexagonal, and occur most in TE.
4) Structural OH content, up to 30% deficient in TE, changes with heating, e.g., to 400°C. In TE it increases (confirmed here by quantitative i.r.). In synthetic OHAp the total amount of structural OH changes little but it does become better ordered. Both results indicate hydroxyl-related defects or disorder in normal TE.

5) Some first results concerning the role of Cl in TE were obtained. The position of Cl in (F,OH,Cl,O) apatites was shown (via several crystal structure refinements) to vary approximately linearly with the amount of Cl present, irrespective of the amount of F and OH present. This permitted extrapolation to predict the position (z=0.38) for Cl in the amount normally found in TE. (This is not the position for Cl in ClAp.) The position of the OH was found also to depend essentially linearly on the amount of Cl present. It was further shown that, as the Cl position along the X-ion column changed, the Ca triangles associated with it, alone, changed size to maintain normal Ca-Cl distances. Thus Cl in tooth enamel must, perforce, produce some variation in Ca(2) ion positions.

6) A micro-twinning phenomenon has been implicated in ClAp which raises the possibility that biological apatite, apparently hexagonal, may really have micro-domains in which the impurity and vacancy content are low enough so the micro-domains are actually monoclinic. This order heterogeneity, correlating with solubility and other properties, is yet another possible aspect of biological apatite to be reckoned with and understand.

7) Single crystals of ClAp have been made CaCl₂ deficient by being heated in vacuum. These are to be studied for themselves and, especially, are to be converted if possible to Ca(OH₂)-deficient OHAp single crystals for further study of Ca(OH₂) loss as a possible contributor to OH deficiency in TE.

8) The CaCl₂ deficiency in ClAp (single crystal) has been shown to produce "satellite" positions for the Ca ions adjacent to vacancies. A Ca(OH)₂ deficiency in TE should then be expected to produce similarly different positions for some of the Ca ions, both Ca(1) and Ca(2), and
thus to contribute to a small apparent disorder in Ca positions in TE.

9) Some advances have been made in our understanding of the thermochemistry and high temperature preparation of carbonate apatite (thanks largely to collaboration with Dr. G. Bonel of Toulouse). Key points are the stoichiometry of the starting OHAp (still not always under control, see (3)) and extreme dryness of the CO$_2$ stream. Neither x-ray nor neutron PFSR analyses attempted for the CO$_3$ location have yet been successful because of second phase contamination and the relative crudeness of the present PFSR program.

10) The structure studies on 5 Cd apatites were completed. The halogens are "too large" to fit in the c period, and they pack in chains with normal halogen-to-halogen distances without control by the coordinating atoms. When the steric strain exceeds some value, a vacancy occurs and a new chain starts. This constitutes a mechanism for sterically-imposed non-stoichiometry and defects which should be considered when large ions substitute for OH in TE.

The process of analyzing the diffraction data for the detailed results involved some advances in analytical method and understanding of diffraction optics which may serve us well in future studies of crystallographic detail related to TE characteristics.

11) Advances were made in the trace element areas through studies of "Pb$_{10}$(PO$_4$)$_6$O" and (Ca,Sr)apatite. In the lead "oxypyromorphite", which turned out to contain substantial amounts of OH, the doubling of the c axis was found to be due to an ordered clustering of O$^-$ and (OH)$^-$ ions. The arrangement and its consequence may have carry-over relevance to TE in which both (OH)$^-$ and O$^-$ occur on the X-ion column (i.e., to the oxyapatite TE model element).

12) The unusual dielectric properties of ClAp (very high and highly anisotropic dielectric constant, $\sim 10^4$) were shown to be based in Cl vacancies. By analogy, this result heightens interest in the possibility of there being similarly highly anisotropic dielectric properties
of the OH-deficient apatite in TE, and especially bones, which plays a role in orienting the crystallites during mineralization.

13) The x-ray pattern-fitting-structure-refinement (PFSR) method has proved to be a powerful analytic tool, greatly increasing the amount of useful information that can be extracted from a powder diffraction pattern—which is the only kind obtainable for TE (and other biological hard tissue). For example, it has permitted the first direct crystal structural study of TE, per se, and analysis of several features in related synthetic apaties. Several opportunities for improving the PFSR program from its present crude form, thereby increasing the amount and detail of the information obtainable about the specimens, have been noted. A re-writing of the program to make it possible to realize many of these opportunities is well along.

AA. c. Detailed Progress Report

1. Overall strategy and principal analytical methods

Although a gap in funding (January through April 1975) produced a severe loss of momentum for a time, good momentum has been regained and substantial progress has been made. Much of the strategy of the project calls for the development of possible atomic-level models for the biological apatite in human tooth enamel (TE) and the assessment of these models with various physical measurement techniques applied to TE itself. The principal sources of detailed model elements are, still, the (x-ray diffraction) single crystal structure studies. The various treatment and assessment methods applicable directly to TE include wet chemical and thermochemical methods. Principal analytical tools applicable directly to TE have been the x-ray PFSR method, quantitative i.r, and deuterizability.

Most promising and potentially most important is the new method for analyzing x-ray powder diffraction data (from TE as well as other naturally polycrystalline materials), the Pattern Fitting Structure Refinement (PFSR) method mentioned in the proposal. The potential impact of this method appears to be large. As with any new method, however, substantial effort must be put into exploring and understanding it and tailoring it for present purposes. See §13a for further discussion of PFSR.
Extensive use has been made of deuteration kinetics and limitations to characterize several aspects of TE and various apatite preparations. Related to ease of diffusion of OH, the results characterize some important diffusion properties including effectiveness of inhibitors such as fluoride. Run at various temperatures from 37°C to 250°C (mostly at 110°C) and pressures, some deuteration runs last a few hours and some several thousand (e.g., 6,000) hours.

Infrared spectroscopy (i.r.) has steadily grown in importance and use; it has now become a major tool, indispensable for the good progress of the project. See §13b of this report.

2. F inhibition of OH diffusion

The question has biological importance because of the known F inhibition of caries incidence coupled with the widely held idea that caries attack involves anisotropic dissolution of the mineral phase; strongly preferential dissolution along the c axis (experimentally shown by others to be usual) would be expected to involve OH diffusion. According to this scenario, then, inhibition of OH diffusion would inhibit caries attack.

A quantitative result for this inhibition has at last been obtained. A quantitative result has been wanted ever since publication of our 1969 paper (Young, van der Lugt and Elliott) pointing out that F substituting for OH did become hydrogen bonded to the neighboring O(H) and thus, being itself more strongly bonded than OH to the Ca ions, should provide an inhibition of OH diffusion.

By studying kinetics of change, with deuteration, of (1) the OH stretch peak at 3572cm⁻¹ in the i.r. spectrum, (2) that perturbed to 3540cm⁻¹ by adjacent F being hydrogen bonded to the perturbed OH, and (3) the corresponding OD stretch peaks, we determined for the specimen studied that those OH's hydrogen bonded to adjacent F's exchanged with OD (i.e., diffused) at only 70% of the rate for the OH not bonded to F. Thus, a significant inhibiting effect of F on OH diffusion has been directly verified and quantified. When similar quantitation has been achieved for a variety of specimens, the then-reliable quantitative data on the inhibitory effect of F should be of possible use in understanding and optimizing fluoride protection from caries.
Studies are continuing on the F effect in synthetic apatites and in TE. Procedures are being tried, with moderate success, to engineer the F content in synthetics and to change it in TE. The samples so treated will then be studied by the deuteration method.

3. Variability of and disorder in OHAp and TE

Deuteration amount, conditions, and kinetics, measured by means of infrared spectroscopy, have proved to constitute a good tool for studying OH diffusibility and for further characterizing both different hydroxyapatite preparations and TE itself.

The first important result of these experiments has been the demonstration that there is considerable variability among hydroxyapatites prepared by different methods. Aqueous preparations (by refluxing of CaHPO₄, and by two different precipitations) are hexagonal (by x-rays) and deuterate relatively easily but not to the stoichiometric limit. High-temperature preparations, whether prepared by high-temperature solid-state reaction or prepared aqueously and then heated strongly (e.g., ≤900°C several hours), are monoclinic and deuterate very slowly. Unheated TE deuterates at least as rapidly as the unheated aqueous preparation. In TE, in particular, the heating increases the amount of structural OH (i.e., showing up at 3572 cm⁻¹) present and decreases the "broad water" component of the i.r. spectrum.

The model pointed to by these data is one of considerable OH "disorder" in the untreated TE and aqueous preparations, perhaps even involving H⁻·O⁻·¹⁻ in the hexagonal axis region. In this disordered environment, OH diffuses rather readily. On heating, much of the initially disordered OH (or that supplied from protein decomposition in the case of TE, or both) settles into the ordered positions for OH in OHAp. (The 3572 cm⁻¹ is then increased, "broad water" is decreased, and deuterizability is decreased.) OH diffusibility is now decreased compared to that in the disordered environment, probably because in the highly ordered (monoclinic) state fewer diffusion routes are available for the outgoing OH and the incoming OD, or other ions, to pass by each other. Thus, if diffusion of OH happens to be a key feature of caries attack, one way of increasing caries resistance would be to produce monoclinic regions in TE! Whether and how this could be done is (at best) debatable at present, but this observation does point a new direction for interest which may or may nor results in anything practical eventually.
That the deuterisation does not take place by recrystallization, but therefore by diffusion, was indicated by the absence of deuteration-induced changes in the breadths or shapes of the profiles in the x-ray diffraction powder patterns made with particular sensitivity for such differences.

A previously unexplained occurrence in the i.r. spectra of F-perburbed and Cl-perturbed OH-stretch peaks on heating of synthetic specimens with no Cl nor F in their preparation materials was shown to be due to F and Cl ions picked up from the furnace environment.

4. OH deficiency in OHAp and TE

In conjunction with the deuteration work, treatment-produced changes in the structural OH content of numerous samples of both synthetic OHAp and TE have been followed by quantitative infrared spectroscopy. The structural OH content of aqueously prepared OHAp has been shown to develop improved ordering (3572 cm⁻¹ peak sharpens) on being heated in air at 1000°C and by simply being kept in water at ~110°C for several hundred hours. However, within an experimental error of ±1%, no increase in area was noted. As was previously known (e.g., LeCeros, 1973) and has currently been verified, the structural OH content (area of 3572 cm⁻¹ line) of TE is increased by heating, even to 400°C. With "on line" i.r. studies in a specially made heating cell, we have shown that the increase of structural OH in TE is accompanied by the evolution of H₂O plus some organic and other species. The work in this area is very active but has not yet reached the stage where many conclusions can be drawn. Mostly, we just have intriguing puzzles right now.

5. F, Cl, and OH structural interactions in apatite-single crystal studies

The role of chlorine in tooth enamel was one of the 3 major tasks area proposed for the current 3 year period.

It has been shown that when F, OH and Cl are present at once, mutual perturbations do occur and a pattern in them has been discerned. Interactions of F, Cl and OH accompanying their intersubstitutions on the 6₃ axis of calcium apatite (nominally Ca₅(PO₄)ₓ) where X=F,Cl and OH, among other possibilities) were determined by means of crystal structure refinements for mineral and synthetic
apatite specimens. The results have been presented at meetings (abstracts 13 & 16) and submitted for publication (paper 10). These "X-ions" interact both structurally and energetically to produce properties not predictable from studies of the end-members (FAp, ClAp & OHAp) alone. Since both F and Cl are present, substituting for OH, in TE their atomic-scale interactions need to be known and understood as a part of understanding the nature and properties of TE and, ultimately, how it might be beneficially modified.

Single crystal structure refinements were newly carried out for 6 different (F,Cl,OH)apatites which, with results from 4 previous refinements, covered the ranges from 0 to 95% of maximum Cl content, 0 to 93% OH, and 0 to 77% F. We particularly thank Dr. E. Kostiner (U. Conn) for synthetic (OH,Cl)Ap crystals of differing Cl/(Cl+OH) ratios. The position of the Cl ion was found not to be fixed at its ClAp value but, rather, to depend approximately linearly on the Cl content almost irrespective of F and OH content. This permitted the prediction of the position of the Cl ion in TE on the basis of the amount present. The prediction (z=0.36 to 0.37 vs 0.44 in ClAp) both assisted and was essentially corroborated by PFSR of TE (abstract no 15). Finding "something" at x=0.37 in the PFSR result alone would not have permitted us to ascribe it to Cl. In fact, without the single crystal studies over the composition range, we would probably have been at a loss to identify with any assurance the "something" occurring at z=0.37. This success is an excellent example of the kind of mutually supportive and amplifying roles (symbiotic and synergistic) played by single crystal studies and direct TE studies, on which much of the project rationale is based.

While the average Cl z coordinate decreases continuously from its stoichiometric chlorapatite value (0.444) to an extrapolated value of 0.39 to 0.40 as the amount of Cl present approaches 0%, the average OH z coordinate diminishes from 0.196 in nearly-stoichiometric hydroxyapatite to ~0.176 in chlorhydroxyapatite in which ~56% of the X-ions are Cl. The dominance of Cl over F in affecting the OH ion position is consistent with the observed infrared spectral effects of greater perturbation of the OH-stretch frequency (3572cm⁻¹ perturbed to ~3540cm⁻¹ by interaction (hydrogen bonding) with F and to ~3495cm⁻¹ by interaction with Cl) and the much greater effect of Cl on the OH (stretch) oscillator strength.
Although the lattice parameter decreases, the Ca(2B) triangle expands as the Cl ion moves closer to it with decreasing Cl content [center-to-apex triangle dimension Δ=2.52Å & z=0.44 for X=95% Cl ranging to Δ=260 & z=0.36 for ~10% Cl] while the Ca(2A) triangle changes little or none.

The correct distinction of Ca(2A) and Ca(2B) was verified by the correlation of (1) Cl site-occupancy with Ca(2B) site-occupancy, (2) Cl z-parameter with Ca(2B) triangle size in a way that maintained normal 2.75(2)Å Ca-Cl distances, and (3) the Ca(2) thermal parameter excess initially found [not distinguishing Ca(2A) and Ca(2B)] with the Ca(2B) site occupancy ultimately determined.

6. Phase transition and microdomain model

It may be recalled that in previous years we have shown that both ClAp and OHAp, previously thought to be hexagonal only, are normally monoclinic when impurity (and, probably, vacancy) content is low. This "new" aspect of OHAp is turning out to have applicability in our understanding of the variability of supposedly pure OHAp (abstract no. 8 and section 3 of this report). Now another unexpected feature has been noted which may further relate to our understanding of the natural material, biological apatite. Largely from optical data, Prener (1967) had reported that ClAp changed from monoclinic to hexagonal on being heated above ~200°C. We now find that, while strong changes do take place in that temperature range, the true monoclinic-to-hexagonal transition does not take place until a much higher temperature, over 400°C, is reached. Further, OHAp behaves rather similarly. (These results are based on high temperature x-ray diffraction data and structure refinements. Data for a full set of structure refinements at several temperatures up to >400°C have been collected and are being analyzed by Dr. Elliott on his computer in London.) What does happen at around 200°C appears to be the onset of a micro-twinning phenomenon which makes the specimen appear optically uniaxial (and hence hexagonal) while the microdomains remain monoclinic. Among other implications of this result is that hexagonal-appearing biological apatite may really have micro-domains in which the impurity and vacancy content are low enough so that the domains are actually monoclinic. This possible order-heterogeneity, correlating with heterogeneity of solubility and other properties, is yet another aspect of the real material (biological apatite) to be reckoned with and understood.
7. **Ca(OH)$_2$ deficiencies - single crystal studies**

It is anticipated that "OHAp" can be deficient in Ca(OH)$_2$ (thus perhaps partially explaining the low Ca/P ratio in TE) just as "ClAp" is known to accommodate deficiency of CaCl$_2$. Precise definition of Ca(OH)$_2$ deficiency is uniquely possible with single crystal x-ray structure studies. The route to such definition appears to lead through CaCl$_2$-deficient chlorapatite crystals subsequently converted, in single crystal form, to "OHAp" which, then, we expect to be Ca(OH)$_2$ deficient.

To date, progress on the Ca(OH) model of the calcium deficiency of TE has been mostly with the analog CaCl$_2$-deficient chlorapatite. We have now successfully made single crystals of chlorapatite CaCl$_2$ deficient (at least, their lattice parameters changed appropriately) by heating them in vacuum. Eventually we hope to convert some of these crystals to hydroxyapatite and find them similarly Ca(OH)$_2$ deficient. That will give us the specimens needed for detailed single crystal studies of the Ca(OH)$_2$ deficiency which will undergird our testing for this effect in (polycrystalline) biological apatite. In the meantime, starting with the particular assistance of Dr. J.C. Elliott in the summer of 1974, we have also undertaken studies of single crystal of CaCl$_2$ deficient ClAp to define the CaCl$_2$-deficient states of "ClAp" in informative structural detail. (See following section)

8. **CaCl$_2$-deficient "ClAp" - single crystal**

The structure of a 0.43 mm diameter melt-grown crystal of CaCl$_2$-deficient ClAp was determined from 1509 reflections measured with MoKa radiation ($\lambda=0.7092\text{Å}$). Lattice constants calculated from 12 reflections were $a=9.615$ and $c=6.77\text{Å}$ with $\sigma=0.002\text{Å}$. These give a value for $x$ of 0.10 in Ca$_{10-x}$(PO$_4$)$_6$Cl$_{2-2x}$ using the lattice constant/chemical composition relationships determined by Prener (J. Solid State Chem., 3, 49, 1971).

The structure was refined with a least squares method followed by Fourier difference maps which showed the presence of satellites close to some of the principal atoms. These were added to the structure and the process was repeated several times in order to find other satellites. Satellites for Cl, Ca(2), O(3), and Ca(1) (two) were found with multipliers in the ranges 0.25 - 0.003. The
multipliers of the Cl indicated a loss of about 15%.

It is thought that the first three satellites arise because they are adjacent to a Cl vacancy. These satellites are for Cl (displaced 0.385Å along the Cl column towards the mirror plane), Ca(2) (displaced 0.385Å toward the Cl column), and O(3) (displaced 0.369Å in a direction making an angle of 78.7° to the P-O(3) bond). The absence of detectable satellites for the other atoms in the PO₄ ion (O(1), O(2) and P) is to be expected because they are more distant from the Cl vacancy. This is also consistent with the fact that the displacement of O(3) is accommodated by a distortion of a bond angle rather than a shift of the PO₄ ion as a whole.

The two Ca(1) satellites originate from Ca(1) ions adjacent to vacancies in the Ca(1) columns. These two satellites are displaced, in opposite directions along the Ca(1) column, by 0.316Å. The unexpected fact that there are vacancies in the Ca(1) columns shows that charge compensation for the loss of Cl requires the loss of Ca(1) (3Å from the Cl vacancy) as well as Ca(2) (adjacent to the Cl vacancy), as we have reported before.

The magnitude of the multipliers of the satellites can give information about the clustering of Cl vacancies. Every Cl vacancy will cause a Ca(2) and O(3) satellite, but only those vacancies adjacent to a Cl ion can cause a Cl satellite. In fact, the multiplier of the Cl satellite is lower than would be expected for isolated Cl vacancies, so an appreciable amount of clustering is indicated.

Analyses of the data on the melt-grown CaCl₂-deficient crystal are still being carried out. When they are completed and the paper is submitted for publication, we will turn our attention to single crystal CaCl₂ made CaCl₂ deficient by being heated in vacuum and to obtaining from it and studying Ca(OH)₂ deficient hydroxyapatite. Thus we will define in detail one possible model for some of the Ca deficiency in TE.

9. Carbonate apatite

The intended effort on carbonate apatite during the current 3 year project period was simply to finish off with CO₃ position data a paper for which the other work was already done.
Substantial efforts were made toward determining the structural locations and role of CO$_3$ substituting (reversibly) for 2(OH) in OHAp and biological apatite. A particular effort involving an initial pool of 60 grams of TE (dense fraction) subdivided into four equal portions, each treated differently, plus an OHAp specimen, has been in progress for several years. Neutron diffraction, x-ray diffraction, infrared and thermochemical data were used to follow the replacement of OH by CO$_3$ and, then, the reverse. At the beginning of the report period we had a draft of a paper on these results but it suffered from two major defects:

1. We really did not know enough about the chemistry of the preparation of pure OHAp and about the thermochemistry of the replacement at (1000°C) of OH by CO$_3$.
2. We still did not have a definitive solution, from the diffraction data, for the location of the CO$_3$.

The first problem has been largely alleviated thanks to Prof. G. Bonel (of Toulouse, France) spending the summer of 1974 with us and, in August 1975 in Toulouse, working with us on the manuscript - on which he is now a co-author. For example, by making the CO$_2$ stream so extraordinarily dry as does Prof. Bonel, one may extend the carbonation beyond the ~85% limit we had encountered. One result is the formation of a new crystalline phase.

With the rather sparse neutron data from our original "carbonated OHAp" and with new x-ray powder data on one of the samples Dr. Bonel prepared here we had expected quickly to determine the CO$_3$ location with the use of our PFSR (pattern fitting structure refinement) program. To date, that has not happened.

The problem, still, is the definitive location of the CO$_3$ substituted for OH in carbonate apatite prepared by exposure to CO$_2$ at high temperature, e.g. 1000°C. The lengthy paper, based on work with 60 gm of TE plus OHAp and several years in the making, awaits this one last fact in order to be ready to be submitted for publication. We have carried out PFSR of both old and new x-ray data on CO$_3$ apatite, but the current program proves not to be sufficiently sophisticated. We are working vigorously, and with every expectation of success, to remove this lack of sophistication. (See 813a). New neutron diffraction data on a specimen newly prepared from OHAp, deliberately not fully carbonated in order that the crystalline phase not be changed, have not yet been analyzed with PFSR -- there is a problem with a second phase. Efforts are underway to prepare a starting CHAp which will not produce so much of the second phase. Our planned modifications of the PFSR program also include the capability for doing PFSR on both the second phase and the major phase at the same time. One or both of these approaches should bring success (finally!).
10. Cadmium apatites and sterically imposed non-stoichiometry

Cadmium apatite (Cd substituted for Ca) are of general interest because of the biological effect (e.g., itai itai disease) of cadmium presumably substituting in small amounts for Ca in biological apatite. The five Cd apatites studied here [Cd₅(PO₄)₃Cl, Cd₅(YO₄)₃I, Cd₅(PO₄)₃Br, Cd₅(AsO₄)₃Br and Cd₅(VO₄)₃Br] turned out to be of unusual interest because of the strange behavior of the over-size halogen ions: They pack in chains with normal halogen-halogen distances, producing successively increasing steric strain with the other coordinating ions until the chain terminates with a vacancy. This constitutes a special cause of non-stoichiometry, one sterically imposed. In biological apatites, one now should watch out for it, especially when large ions substitute for OH and possibly when (and where, in the apatite crystals) smaller ions substitute for Ca. Thus, Cd is a possibly important minor substituent for Ca. But these studies may also relate to OH deficiencies and substituitions.

The compounds being newly reported on are Cd₅(AsO₄)₃Br, Cd₅(PO₄)₃Br, Cd₅(YO₄)₃Br and Cd₅(VO₄)₃I. They are approximately isostructural with fluorapatite, Ca₅(PO₄)₂F, and the positional parameters of the non-halogen atoms are very similar. The halogen atoms, however, do not occupy the ideal positions +0,0,1/4 nor any unique positions +0,0;z) on the hexad axis. Relative to the oxygen atoms they are present in less than stoichiometric amounts, the deficiency increasing from about 8% to 26% in the order in which the formulae are listed. This effect appears to result from steric hindrance, the usual ionic diameters of the halogens exceed 1/2C by 10-20%. Refinements of the crystal structures (final R's about 0.05) indicate that the formulae should be written Cd₅₋ₓ(YO₄)₃ₓ₋₄ₓ₂, where x can be as large as 0.13 in one (the iodide) case.

Direct determination of the probability distribution of the positions of the halogens has been attempted in three ways: (i) Fourier atomic-center density syntheses, (ii) least-squares refinement of the occupancy factors of a multiplicity of sites uniformly spaced along the c axis, and (iii) fitting of postulated distribution functions to the 'observed' structure factors corresponding to halogen centres only. All methods are similarly limited by the rather low resolving power afforded by the reflections in the accessible volume of reciprocal space. The results are consistent with a 'chain' model in which the center of
each chain occupies the modal position 0,0,1/4 or 0,0,3/4; atoms in succeeding half cells deviate further and further from this position, until finally the steric strain is relieved by the occurrence of a vacancy, after which a new chain begins. For all five compounds investigated, qualitative agreement is achieved with a uniform distribution of atomic centers over a range of δ on each side of the modal positions ±(0,0,1/4), with δ ranging from 0.04 to 0.2. The rather remarkable result, that the halogens are more influenced by each other than by their surroundings in the crystals, is thus quantitatively verified. One implication of interest is the production of non-stoichiometry as a way of accommodating, in the apatite structure, over size ions.

The process of analyzing the crystal structure data on the five Cd apatites in such a way as to be reasonably sure of the strange halogen distribution (and hence of its implications) turned out to be a significant effort and one that took us into deep consideration of the diffraction physics of the situation. This rather substantial effort has now been written up in (only!) two papers, drafts of which were reported last year. The papers have now been finished and accepted for publication (no.'s 7 & 8 on the list). Their abstracts are appended.

Prof. A.J.C. Wilson (Birmingham, England) spent about four weeks with us in November and December 1975 working intensively on, and completing, the second of the two papers. We are pleased to have this big job done. We are grateful to the Royal Society for providing his airfare, to the William Waldorf Astor Foundation for providing his subsistence expenses, and to Prof. Wilson for donating his time.

11. Other substitutions ("Trace" elements)

Among the substitutions for calcium that are of principal interest are Sr, Pb, Na, Mg, K, Mn and Zn.

a. Lead "oxypromorphite"

An effort which touches on the task areas of oxyapatite and of minor substituents - Pb, is the determination of the crystal structure of an "oxypromorphite", presumably Pb₁₀(PO₄)₆·0 but actually closer to Pb₁₀(PO₄)₆·0₁−ₓ(OH)₂ₓ where x ≈0.3. The single crystals were kindly supplied by Prof. H. Wondratschek.
A point of interest is the reason for the doubling of the c axis thought by Wondratschek (1963) to be due to clustering of the axial oxygen atoms but now seen to be more probably due to clustering of O's and OH's along the axis. The arrangements of the O's and OH's, and their consequence, may have carry-over relevance to the "oxyapatite" component, if any, of tooth enamel.

Work with the final resolution of the structural detail in \( \text{Pb}_10(\text{PO}_4)_6(\text{O},\text{OH}) \) is stalled on a lack of uniqueness of the O positions that seem to fit the available data within experimental error. At this point we are not sure whether the difficulty can be overcome by a different calculational approach or whether more extensive x-ray data (difficult, as crystals are very small) will be required.

b. \((\text{Ca},\text{Sr})\text{Apatite}\)

Three batches of \((\text{Sr,Ca})\text{Ap}\) crystals have been grown in which the ratio of Sr to Ca is about 1/70, 1/20, and 2/5, respectively. Three dimensional single crystal x-ray data have been collected for crystals from the first and third batches. Data collection for the other is in progress. Hopefully, detailed structure refinement covering the range of substitutions will give us some insight into the structural effects of the introduction of the Sr, perhaps much as the \((\text{F,Cl,OH})\text{Ap}\) studies gave us for Cl (§3.4). That, in turn, should aid understanding of structurally-related changes in properties such as solubility, crystallizability, and preferential exclusion of Sr on recrystallization - probably the fortunate self-purging process by which bone can rid itself of \(^{90}\text{Sr}\).

12. Dielectric properties of \(\text{ClAp}\)

Dielectric Properties of Chlorapatite is the title of the Ph.D. (Physics, Dissertation which E.O. Rausch has now completed and turned in. A copy of the summary of the Thesis (dissertation) is appended. Although chlorapatite does not occur per se in biological apatite, in many of its properties it is analogous to hydroxyapatite (and can be obtained much more easily in a form suitable for study).

Determination of the complex dielectric constant as a function of frequency \((10^2 \text{ to } 10^7 \text{ Hertz})\), temperature \((25^\circ \text{ to } 300^\circ \text{C})\), \(\text{CaCl}_2\) deficiency (up to 20%), plus some determinations with Cl partially replaced by F or by OH, and hysteresis-loop observations have led to a Cl-vacancy F-inhibited model.
It is an extended Debye relaxation model based on some Cl-ions being able to move between potential minima at $z = 1/2 \pm \delta$ (δ≈0.06Å), because of vacancies, and involving a spread of relaxation times in the $10^{-6}$ sec region. A few (e.g. 2-4) per cent of the Cl ions need to be missing (and are) in order to explain the dielectric properties observed. Thus, some departure from stoichiometry, such as would be anticipated for biological materials, is required for large effects. The role of impurities other than F is not known; ≤10% F substituted for Cl reduced the dielectric constant in the c direction by a factor of ~100.

A particular point of biological interest arises from the bioelectric effect on bone growth. The point to be understood from studies of the dielectric properties of apatites is why and how electric fields do influence the deposition of apatite crystals and, possibly, their orientation. To the extent that chlorapatite (ClAp) is analogous to biological "hydroxyapatite", the answer is that ClAp has a very unusually high (e.g., 40,000) dielectric constant in one direction only. The high dielectric constant will cause it (e.g., small crystals) to experience a transport force in an inhomogeneous electric field (which the bioelectric source may be expected to produce). Further, the great anisotropy (∼10⁵) in the dielectric constant will result in an orienting force. Thus, both transport and orientation of apatite crystals in bioelectric fields can be accounted for on the basis of the dielectric character found for chlorapatite, if the defect hydroxyapatite constituting biological apatite behaves similarly. The interesting dielectric properties of ClAp, the atomic scale mechanism of which has now been elucidated, require some defects in the form of Cl ion vacancies for their occurrence. For extending the analogy to biological "hydroxyapatite" this is encouraging, as biological hydroxyapatite certainly has plenty of defects. However, in the ClAp studies the substitution of small amounts of F ion destroyed the unusual dielectric property. Probably certain kinds of other impurities would also. Thus there may be an indicator here that clinical (in vivo) investigation of the effect of specific impurities on bioelectrically stimulated bone growth (for example) might be worthwhile. Probably some in vitro experiments might most fruitfully be performed first.
13. Tools
   a. X-ray pattern-fitting-structure-refinement (PFSR)

The PFSR (Pattern-Fitting-Structure-Refinement) technique has been shown to be very powerful in revealing atomic details of apatite from powder diffraction patterns. Previously unattainable information about atomic locations and arrangements (which strongly determine many important chemical and physical properties) is offered by this new technique which permits essentially full utilization of the information present in a powder diffraction pattern, whether or not it occurs in separately measurable Bragg peaks. Least-squares adjustments of crystal structural and profile parameters are made possible. Originally developed (Rietveld, 1967, 1969) and successfully used (e.g., Hewatt 1973, Fender et al.,


for neutron powder diffraction patterns, PFSR has now been extended by us to the x-ray case and applied to apatites. X-ray powder data on synthetic fluorapatite yielded highly precise lattice parameters ($a=9.3655(3)\text{Å}$, $c=6.8818(3)\text{Å}$) and the result that no atom position differed from single-crystal results by more than 3σ. Synthetic chlorapatite (monoclinic) parameters resulting from PFSR were $a=9.6347(9)\text{Å}$ and $c=6.7623(7)\text{Å}$ with $b=2a$ and $\beta=120^\circ$. Although refinement of atomic positions in ClAp is presently frustrated by a pseudo-symmetry problem, excellent pattern matching is nonetheless obtained. Several minor things have been done to improve the stability and convergence of the program and to improve its applicability. For example, a new matrix inverter has been written, a pattern-stripping feature has been added, and pseudo rigid-body constraints were added in order to increase the power of the method for locating the CO$_3$. That particular effort, however, requires major improvements (planned).
At this point we have had both successes and failure with PFSR and are currently working vigorously on improving it. A first paper on the method, discussing its trial application to 5 different materials, has now been accepted for publication (paper no. 9 in the list). Those and further experiences with PFSR were presented at the March ACA meeting (abstract no. 14). A particularly important success; the first direct structure analysis of TE, will be presented at the next AADR meeting (abstract no. 15). Abstracts of the written paper and the two oral presentations are appended.

The PFSR successes are exhilarating, but they are not complete - for example, final fits are not as good as they could be in many cases. It is clear that our present approach is realizing only a part of the potential and that there are several obvious things to be done at once to improve matters (many are mentioned in paper no. 9). For the project to benefit from more of the potential (particularly that relating to better definition of fine details such as are crucially important in our understanding of biological apatite as distinct from idealized apatite), we are currently writing a new version of the PFSR computer program which will be more powerful, more flexible, and more surely modifiable and usable than the present one. Although such a rewrite takes a considerable effort (e.g., of the order of 9-12 man months), (1) we found that attempts to modify the existing program into needed form threatened to be even more costly and (2) it is very important to this project that the PFSR method be available in its most effective form. Just as two examples of need, the improved PFSR is needed (1) for critical assessment of the possibility of a bi-modal distribution of crystallite sizes in TE (see abstract no. 15) and (2) for the firm location of \( \mathrm{CO}_3 \) in carbonate apatite. (Present results are inconclusive, in part because the available profile functions are not adequate - see paper no. 9).

b. **Infrared spectroscopy**

Infrared spectroscopy is the method with which we can measure, quantitatively, the progress of deuteration and some of its characteristics such as diffusion rates for different \( \mathrm{OH} \) locations. It is used to follow changes in amount and environment of \( \mathrm{CO}_3 \) and \( \mathrm{CO}_2 \) on treatment (esp. heating) of TE and apatite, of
water, and of X-ion-column occupancy effects on phosphate vibrations. It is used to study changes in the ordering of the OH's and other groups. It is used to make dynamic studies of the gases evolved when TE and apatite are heated. All of this requires a first-rate instrument and a highly skilled and ingenious user. We have been fortunate in having access to a Perkin-Elmer 621 instrument belonging to another department. We greatly appreciate their cooperation, but there are two problems with this arrangement. One is that we are now the major user of the instrument and when that department's workload for the instrument increases, as it will, our second priority (presuming that, being "free-loaders", we can even maintain that) will not give us sufficient access to the unit. A second problem is that we can not change the configuration or operation of the instrument nor fill it with special adaptors and controls to best serve our particular purposes.
A4d. PUBLICATIONS

(i) Full papers published or submitted for publication during the reporting period. (Abstracts provided at end of list)


* Listed on last report as being in press.


(ii) Dissertation (Abstract at end of list)


(iii) Published abstracts of presentations at scientific meetings. 
(Copies follow list)


Structure Refinement and Random Error Analysis for Strontium 'Chlorapatite', Sr₅(PO₄)₃Cl

BY K. SUDARSANAN AND R.A. YOUNG
Georgia Institute of Technology, Atlanta, Georgia 30332, U.S.A.

(Received 10 September 1973; accepted 26 December 1973)

The crystal is hexagonal, \( P6_3/m \), with \( a = 9.859 (1) \) and \( c = 7.206 (2) \) Å. Least-squares refinements (1174 independent diffractometer-measured reflections, 42 parameters, Mo Kα radiation, corrections for absorption and extinction, simultaneous diffraction effects minimized) led to \( R(F) = 0.034 \) and \( wR(F^2) = 0.044 \). The general structural features are the same as those of fluorapatite and hydroxyapatite except for the position of the chlorine atom, which is at \( 0,0, \frac{1}{2} \), midway between the two Sr triangles on the mirror planes at \( z = -\frac{1}{2} \) and \( z = \frac{1}{2} \). Error analysis carried out with normal probability plots and correlation-testing plots showed that over and above the counting statistical errors and instrument instability there was an additional random error, of the order of \( 5\% \) of \( \sqrt{R} \), of unknown origin. Also encountered with other specimens, and thought not to be due to crystal dimension and absorption coefficient errors, this additional error might be due to crystal inhomogeneity with respect to diffraction.

COMPOSITIONAL ANALYSIS OF APATITES WITH LASER-RAMAN SPECTROSCOPY:
(OH,F,Cl)APATITES

D. C. O'SHEA, M. L. BARTLETT* and R. A. YOUNG
Georgia Institute of Technology, Atlanta, Georgia 30332, U.S.A.

Summary—Feasibility of analyses for OH and other components in regions as small as \( 20 \) \( \mu \)m across has been demonstrated with a view toward analysis of spatial variation of tooth composition. Laser-Raman spectra of fluorhydroxyapatite and chlorhydroxyapatite with halide compositions corresponding to up to 40 per cent replacement of hydroxyl ions are reported. The lattice mode region below \( 300 \) cm\(^{-1} \) for the three pure apatites has also been newly observed, that for hydroxyapatite being reported for the first time known. Several line intensities or frequencies are viable candidates for use in quantitative analysis of the kind and degree of halide intersubstitution, e.g. F for OH in tooth enamel. Substitution of Cl rather than F for OH can be distinguished by line shifts in the lattice mode region and by changes in the ratio of certain phosphate-mode line intensities. With present data, sensitivities of 5 per cent F for OH (e.g. 612 597 cm\(^{-1} \) intensity ratio of approximately 2 per cent CI for OH (612 451 cm\(^{-1} \) intensity ratio), and 5 per cent deficiency of OH (553 cm\(^{-1} \) line intensity) are indicated. Better sensitivity can be anticipated with refined techniques. A trial application to human tooth enamel showed, through large amounts of visible-light induced fluorescence, apatite-like spectra exhibiting both broadening and mode-frequency shifts.
SOME ASPECTS OF CRYSTAL STRUCTURAL MODELING OF BIOLOGICAL Apatites

R. A. YOUNG
Georgia Institute of Technology
Atlanta, Georgia 30332, U.S.A.

Summary

Through discussion, illustrations and examples an effort is made to provide the background for appreciation of the nature and importance of atomic scale mechanisms of physico-chemical properties as determinable from precise studies of crystal structural details.

The crystal structures of fluorapatite (FAp) hydroxyapatite (OHAp) and chlorapatite (ClAp) are reviewed in graphic detail.

The fact that biological apatite is not OHAp but may be modeled usefully by multiply substituted forms of "OHAp" is pointed out: some substitutions were studied in atomic scale, particularly in the case of apatite of biological interest.

Résumé

Dans le cadre d'une discussion illustrée par des schémas et des exemples on tente d'apporter des données fondamentales qui permettent d'apprécier les relations entre les phénomènes à l'échelle atomique et les propriétés physico-chimiques: ces relations sont mises en évidence à partir de détermination très précises des données structurales.

On décrit en détail graphique les structures de la fluorapatite (FAp), de l'hydroxyapatite (HAp), de la chlorapatite (ClAp).

On montre à l'aide de modèles que l'apatite biologique, qui n'est pas l'hydroxyapatite, dérive peut être de cette dernière par diverses substitutions que l'on étudie à l'échelle atomique en considérant en particulier les apatites d'intérêt biologique.
Fluorine-Chlorine Interaction in Fluor-Chlorapatite

P. E. MACKIE AND R. A. YOUNG

Georgia Institute of Technology, Atlanta, Georgia 30332

Received December 11, 1973

When fluorine is partially substituted for chlorine in chlorapatite, steric interactions between the F and Cl ions produce effects not directly predictable from the properties of the end members, fluorapatite and chlorapatite, alone. The proximity of the remaining chlorine ions causes some of the substituting fluorine ions to be located +0.6 Å from their normal sites (0, 0, 0) and (0, 0, 1) on the halogen ion column. Some of the chlorine ions are similarly shifted >0.2 Å farther away from (0, 0, 1). The details of the displacements have been determined from least-squares analyses of X-ray data from synthetic single crystals. Two fluor-chlorapatite compositions were used, ~14% and ~34% substitution of F for Cl, with excess halogen becoming incorporated to raise the F : (F + Cl) ratios to 0.17 and 0.41, respectively. The substitution models developed are capable of explaining (i) the nonlinear effects of the fluorine-chlorine substitution, and (ii) the initial stabilization and later inhibition of the monoclinic phase, with respect to the hexagonal phase, with increasing substitution of fluorine into the chlorapatite structure, and (iii) in part, the occurrence of halogens in excess of the stoichiometric 2 per unit cell.

Summary

Hydroxyapatite prepared by heating flux-grown chlorapatite in steam at 1 200 °C for two weeks has a monoclinic space group P21/ b. The structure of such a specimen determined by X-ray diffraction methods is described.

The distortions of the monoclinic hydroxyapatite structure from the very closely related hexagonal one usually found in apatites are very similar to those distortions that have been found in monoclinic chlorapatite.

Résumé

L'hydroxyapatite obtenue par chauffage, dans un courant de vapeur d'eau à 1 200 °C durant deux semaines, de monocristaux de chlorapatite préparée par la méthode du flux présente une structure monoclinique (groupe spatial P21/ b). Sa structure établie par la diffraction des rayons X est décrite.

Les distorsions que présente l'hydroxyapatite monoclinique, par rapport à la structure hexagonale généralement observée pour les apatites, sont semblables à celles qui interviennent dans la chlorapatite monoclinique.
Biological Apatite vs Hydroxyapatite at the Atomic Level

R. A. Young

SUMMARY

Known differences in chemical content of biological apatites, specifically the dense (sp.g. > 2.95) portion of human tooth enamel (TE), and of stoichiometric hydroxyapatite (OHAp) imply atomic-scale crystal-structural differences, via major and minor substitutions, which can impart very different characteristics to the two materials. Further, some substitutions are shown to produce important effects not predictable from study of pure materials alone. A number of crystal-detail differences between TE and OHAp, both at room temperature and in response to heating (which occurs to some degree locally in hard tissue in vivo as a result of grinding, laser action, etc.), are tabulated. They include CO₂, content and incorporation, lattice parameters, water content, non-OHAp phases formed on heating, structural OH deficiency, and hydrogen-bonding of F and Cl "impurities" to OH. The significance of these differences is such that it is clearly misleading to speak of tooth enamel, and by inference other biological apatites, as "hydroxyapatite" without considerablequalification of the statement. The differences between biological apatite and OHAp are, in fact, of greater current interest and probable biological significance than are the similarities.
The Structures of Some Cadmium 'Apatites'

Cd$_5$(MO$_4$)$_3$X. I. Determination of the Structures of Cd$_5$(VO$_4$)$_3$I

Cd$_5$(PO$_4$)$_3$Br, Cd$_5$(AsO$_4$)$_3$Br and Cd$_5$(VO$_4$)$_3$Br

K. Sudarsanan and R. A. Young
Georgia Institute of Technology
Atlanta, Georgia 30332, USA

and

A. J. C. Wilson
The University of Birmingham
Birmingham, B15 2TT
United Kingdom

ABSTRACT

The compounds are approximately isostructural with fluorapatite, Ca$_5$(PO$_4$)$_3$F, (P6$_3$/m, Z=2) and the positional parameters of the non-halogen atoms are very similar for all. The halogen atoms, however, do not occupy the ideal positions $\pm$$(0,0,1/4)$ nor any unique positions $\pm$$(0,0,z)$ on the hexad axis. Relative to the oxygen atoms they are present in less than stoichiometric amounts, the deficiency decreasing from about 27% for the iodide to ~8% for the arsenate bromide. This deficiency appears to result from steric hindrance, the usual ionic diameters of the halogens exceeding $\frac{1}{2}c$ by 10-20%. Refinements of the crystal structures of the title compounds and of Cd$_5$(PO$_4$)$_3$Cl (final R's about 0.05) indicate that the formulae should be written Cd$_{5-x}$(MO$_4$)$_{3-2x}$X$^x$, where $x$ can be as large as 0.13 in one (the iodide) case.
The Structures of Some Cadmium 'Apatites'

\[ \text{Cd}_5(MO_4)_3X \cdot \text{II. The Distributions of the Halogen Atoms in} \]
\[ \text{Cd}_5(VO_4)_3 \text{I, Cd}_5(PO_4)_3 \text{Br, Cd}_5(AsO_4)_3 \text{Br, Cd}_5(VO_4)_3 \text{Br, and Cd}_5(PO_4)_3 \text{Cl}. \]

A. J. C. Wilson
The University of Birmingham
Birmingham, B15 2TT
United Kingdom

and

K. Sudarsanan and R. A. Young
Georgia Institute of Technology
Atlanta, Georgia 30332, USA

ABSTRACT

Many cadmium 'apatites' are 10 to 20% halogen deficient, with the halogen atoms distributed over a range of positions on the hexad axis instead of occupying the ideal positions \( \pm (0,0,\frac{1}{4}) \). Direct determination of the probability distribution of their positions has been attempted in three ways:

(i) Fourier atomic-centre density syntheses, (ii) least-squares refinement of the occupancy factors of a multiplicity of sites uniformly spaced along the \( c \) axis, and (iii) fitting of postulated distribution functions to the 'observed' structure factors corresponding to halogen centres only. All three methods are limited similarly by the resolving power afforded by the reflections in the accessible volume of reciprocal space. The results from all three methods are consistent with a 'chain' model in which the centre of each chain occupies the modal position \( 0,0,\frac{1}{4} \) or \( 0,0,\frac{3}{4} \). Being 'oversize' (diameter > \( \frac{1}{2} c \)), halogen ions in succeeding half cells are forced to deviate further and further from this modal position, until finally the steric strain is relieved by the occurrence of a vacancy, after which a new chain begins.
APPLICATION OF THE PATTERN-FITTING-STRUCTURE-REFINEMENT
METHOD TO X-RAY POWDER DIFFRACTOMETER PATTERNS

by

R. A. Young, P. E. Mackie and R. B. Von Dreele,
Georgia Institute of Technology, Atlanta, Ga. 30332
and Arizona State University, Tempe, Arizona 85281

ABSTRACT

The whole-pattern least-squares fitting method (herein called the
pattern-fitting-structure-refinement, PFSR, method) developed by Rietveld
and used by many with neutron powder data has been extended to utilize
x-ray powder diffractometer data. Examples of PFSR for specimens in five
different space groups are given. Structural parameters generally agree
within 2σ of those from single crystal results where available. Atom positions
and site occupancies were determined for LaPo₄, Ca₃(PO₄)₂F, and quartz.
R(pattern) factors generally ranged from 9 to 20% while R(Bragg) factors
were a few per cent lower. Reflection profiles were represented by either
Gaussian or Cauchy functions; better representations are shown to be needed
with an expected result of improved sensitivity accompanying lower R factors.
Possibilities for improved pattern-stripping for minor phase study via PFSR
of the major phase are exhibited. Remarkably precise lattice-parameters,
e.g. 1 part in 35,000 from data all below 2θ<77° in the fluorapatite case,
and parametric characterization of the diffraction broadening of the Bragg
profiles are obtained as additional benefits.
Interactions of F, Cl and OH in Apatites

K. Sudarsanan and R. A. Young
Georgia Institute of Technology
Atlanta, Georgia 30332 U.S.A.

ABSTRACT

Structural interactions of F, Cl, and OH accompanying their intersubstitutions on the 6_3 axis of calcium apatites \( \text{Ca}_5(\text{PO}_4)_3X \), where \( X=F, \ Cl \& \ OH \), with space group \( P6_3/m \) have been determined by means of crystal structural refinements for six mineral and synthetic specimens of differing \( X \)-ion contents plus reported results for the end-members. The \( z \) positional parameters of both Cl and OH positions are primarily sensitive to and depend roughly linearly on the fractional amount of chlorine present. The dominance of Cl over F in affecting the OH ion positions is consistent with the observed infrared spectral effects of greater perturbation of the OH stretch frequency by Cl.

As the relative Cl content decreases, the Cl ions move closer to the planes of the associated Ca triangles, which expand to maintain the normal Ca-Cl distance, while the Ca triangles associated with other \( X \)-ions remain relatively unchanged. The pattern found leads to a predicted \( z \) positional parameter of 0.36 to 0.37 for the Cl in human tooth enamel, contrasting with 0.44 in chlorapatite.
SUMMARY

Most dielectrics found in nature have dielectric constants between 1 and 10 and rarely greater than 100. Nearly stoichiometric chlorapatite (Ca₅(PO₄)₃Cl) is, therefore, a material with unusual dielectric properties because it exhibits a dielectric constant \( > 10^4 \), a dielectric anisotropy \( > 10^3 \), an apparent ferroelectric character and time-dependent d.c. conductivity. At 1000 Hz and 25°C the real part of the dielectric constant \( (\varepsilon'') \) is \(-10^6\) and the imaginary part \( (\varepsilon'') \) is \(-10^3\) parallel to the \( c \) axis while < 10 and < 0.01, respectively, perpendicular to \( c \).

The purpose of this research was first to measure and then to explain these dielectric properties on the basis of a detailed atomic scale mechanism. Both dielectric and x-ray measurements of several kinds were employed.

Dielectric Studies

Measurements of the dielectric constants, \( \varepsilon' \) and \( \varepsilon'' \), as a function of frequency (10²-10⁶ Hz), temperature (25-400°C) and applied-field dependence were explored in "pure" and fluorine-doped forms of chlorapatite. The substitution of only 4% of the Cl by F ions reduced both \( \varepsilon' \) and \( \varepsilon'' \) parallel to \( c \) (at 26°C and 1000 Hz) by a factor of 100. This evidence verified that the high dielectric constant is directly associated with the Cl ions.
reflections to determine the persistence of monoclinic ordering and the domain size for it. The transition reported by others near 200°C has been shown not to be, as they thought, the monoclinic to hexagonal phase transition. Instead, that transition is herein predicted to occur at a temperature between 400 and 500°C. The 200°C transition appears to be associated with the breaking up of the monoclinic long-range ordering of the crystal into microdomains perhaps no larger than 60 Å.

On the basis of these results for chlorapatite, a possible mechanism is proposed for the reversal of OH dipoles in hydroxyapatite involving an O2- defect and leading to possibly similarly interesting dielectric properties in that material.

A vacancy defect model is advanced which successfully accommodates all of the above phenomena. It involves (a) the migration of Cl vacancies along the Cl chain and (b) field reversible shifts (≈ 0.8 Å) of Cl ions along the chain direction in double wells made available by the occurrence of Cl ion vacancies. The activation energy of the Cl shift (< 0.2 eV) and the dipole density (e.g., < 1 per 100 cells) were also determined from the data.

Although the θ versus E hysteresis loop observed in chlorapatite is suggestive of a ferroelectric character, the structure of the bulk of this material is centrosymmetric, which symmetry is not consistent with the occurrence of ferroelectricity. As a result the hysteresis loop was not identified as a bulk property of chlorapatite but instead it was associated with the Cl shift which in turn is indirectly associated with the small number of vacancy defects in the crystal. The term pseudo-ferroelectric is therefore used for this chlorapatite material.

The d.c. conductivity was ascribed to vacancy migration and the subsequent neutralization of the vacancies near the electrodes.

X-Ray Studies

In order to better understand, both, the nature of the dielectric properties in CIaP and the mechanism of the transition occurring near 200°C x-ray studies were initiated to investigate the temperature dependence of (a) the r.m.s. thermal vibrational amplitude of the Cl ion in the c direction, (b) the equilibrium position of the Cl ion, and (c) the intensities and breadths of some of the "monoclinic" x-ray
INTERACTIONS OF F, Cl, AND OH IN Apatite
Sudarsanan and R. A. Young, Georgia Institute of Technology, Atlanta, Georgia.

Interactions of F, Cl and OH accompanying their intersubstitutions on the 6, axis f calcium apatite (nominally Ca₅(PO₄)₃X where X=F, Cl and OH, among other possibilities) ave been determined by means of crystal structural refinements for several mineral and synthetic apatite specimens. The findings are expected to be applicable to biological patite, such as that of human tooth enamel, in which these three ions are present simul-
aneously. The z positional parameters of both Cl and OH are primarily sensitive to and eloped roughly linearly on the fractional amount of chlorine present, even though the OH osition is known to be affected by hydrogen bonding to neighboring F ions. The average 1 z coordinate decreases continuously from its stoichiometric-chlorapatite value (0.444) o an extrapolated value of 0.39 to 0.40 as the amount of Cl present approaches 0%. The average OH z coordinate diminishes from 0.196 in nearly-stoichiometric hydroxyapatite o -0.176 in a chlorhydroxyapatite in which ~56% of the X-ions are Cl. The dominance of Cl over F in affecting the OH ion position is consistent with the observed infrared spectral effects of greater perturbation of the OH-stretch frequency (3572 cm⁻¹ perturbed to 3540 cm⁻¹ by interaction (hydrogen bonding) with F and to 3495 cm⁻¹ by interaction ith Cl) and the much greater effect of Cl on the OH (stretch) oscillator strength.

This work has received financial support from the US Public Health Service hrough NIH-NIDR Grant DE-01912.

Topic Sentence:
Mutual perturbations of "halogen" ions do occur which could not be predicted from studies f end members alone and a pattern in them has been discerned.
Defect Origin of Unusual Dielectric Properties of Chlorapatite. E. O. RAUSCH and R. A. YOUNG*
Georgia Institute of Technology, Atlanta, Ga.
The high and highly anisotropic dielectric constant (>10,000 parallel to and \(<10^6\)) and apparent ferroelectric character (Elliott & Young, 1968) of chlorapatite are of special interest because of the detailed crystal structural similarity of chlorapatite, \(\text{Ca}_5(\text{PO}_4)_3\text{Cl}\), to hydroxyapatite, \(\text{Ca}_5(\text{PO}_4)_3\text{OH}\), and the fact that growth of hard tissue is strongly influenced by electric fields or currents. (A high dielectric constant, whether or not of polar origin, could be important in the apatite transport and orientation mechanisms).

Determination of the complex dielectric constant as a function of frequency (10 A to 10 \(^7\) Hertz), temperature (25\(^\circ\) to 300\(^\circ\) C), \(\text{CaCl}_2\) deficiency (up to \(<20\%\)) plus some determinations with Cl partially replaced by F or by OH and hysteresis-loop observations have shown that growth of hard tissue is strongly influenced by electric fields or currents. (A high dielectric constant, whether or not of polar origin, could be important in the apatite transport and orientation mechanisms).

Determination of the complex dielectric constant as a function of frequency (10 A to 10 \(^7\) Hertz), temperature (25\(^\circ\) to 300\(^\circ\) C), \(\text{CaCl}_2\) deficiency (up to \(<20\%\)) plus some determinations with Cl partially replaced by F or by OH and hysteresis-loop observations have led to a Cl-vacancy F-inhibited model. It is an extended Debye relaxation model based on some Cl-ions being able to move between potential minima at \(z = 1/2 + \delta\) and \(z = 1/2 - \delta\) \((\delta \sim 0.06\) cm\) because of vacancies and involving a spread of relaxation times in the 10\(^{-6}\) sec region. A few per cent of the Cl-ions need to be missing (and are) in order to explain the dielectric properties observed. Thus some departure from stoichiometry, such as would be anticipated for biological materials, is required for large effects. The role of impurities other than F is not known; <10\% F substituted for Cl reduced the dielectric constant in the \(c\) direction by a factor of \(<100\).

Special precautions were required to get values characteristic of the material rather than of absorbed water and of organic films from painted-on specimen electrodes.

This work has received financial support through NIH-NIDR Grant DE-01912.
Atomic Details of Apatites from Powder Diffraction Patterns. P. E. HACKIE* and R. A. YOUNG.
Georgia Institute of Technology, Atlanta, Ga.

Previously unattainable information about atomic locations and arrangements (which strongly determine many important chemical and physical properties) is offered by the new Profile-fitting Structure Refinement (PFSR) technique which permits essentially full utilization of the information present in a powder diffraction pattern, whether or not it occurs in separately measurable Bragg peaks. Least-squares adjustments of crystal structural and profile parameters result. Originally developed (Rietveld, 1967, 1969) and successfully used (e.g. Hewatt 1972, 1973, Fender et al, 1974, 1974, 1974) for neutron powder diffraction patterns, PFSR has now been extended to the x-ray case and applied to apatites. X-ray powder data on synthetic fluorapatite yielded highly precise lattice parameters (a=9.3655(3)Å, c=6.8818(3)Å) and the result that no atom position differed from single-crystal results by more than 0.3Å. Synthetic chlorapatite (monoclinic) parameters resulting from PFSR were a = 9.6374(9)Å and c = 6.7623(7)Å with b=2a and α = 120°. At the present stage, refinement of atomic positions is frustrated by a pseudo-symmetry problem but excellent pattern matching is nonetheless obtained. PFSR with a neutron powder diffraction pattern of synthetic "hydroxyapatite", in which the OH has been largely replaced by CO3 at high temperature, showed that the CO3 was in the "halogen ion channel", as expected, and indicated that further PFSR with the appropriate space group and these or better data will lead to a definitive determination of the CO3 location and orientation.

This work has received financial support through NIH-NIDR Grant DE-01912.
APPLICATION OF PROFILE-FITTING-STRUCTURE-REFINEMENT METHOD TO X-RAY POWDER DIFFRACTION DATA. R. A. Young and P. E. Mackie, Georgia Institute of Technology, Atlanta, Georgia 30332.

The Profile-Fitting-Structure-Refinement (PFSR) method (i.e., point-by-point fitting in a least-squares sense in contrast to fitting of individual integrated Bragg intensities) previously applied by others to neutron diffraction data has been applied to x-ray powder diffraction data (obtained by a step-scan technique). With a sample giving a sharp pattern (fluorapatite, full width at half height (FWHM) of the 211 peak was 0.15°) an R factor (based on 115 |F|^2's) of 9.7% was obtained. 28 parameters were varied (atomic coordinates, site occupancies, overall scale factors, and half-width parameters; not thermal parameters) and 1853 intensity data were used from 2θ < 78° with CuKα radiation. The standard deviations indicate a precision of approximately 0.01Å in the atomic coordinates and 2% in the site occupancies (compared to 0.001Å and 0.5%, respectively, in the structure refinements with single-crystal data from a larger range in (sin θ)/λ).

Remarkably precise lattice parameters are also obtained as a spin-off benefit from PFSR. With fluorapatite and chlorapatite samples, precisions of 3 parts in 100,000 and 1 part in 10,000, respectively, were obtained. Because PFSR requires "best-fit" for the whole profile envelope and not just the position of the maximum, surprisingly good lattice-parameter precision can be obtained even from badly smeared powder patterns. In one such case (FWHM = 1.1° at 31° (2θ)) with Cu radiation in which only data below 2θ = 90° were used, lattice parameters with a precision of 1 part in 2,000 were obtained.

In the present work, the overall profile has been represented by a gaussian (the α doublet simulated by two gaussians). Although not correct, this is acceptable when the diffraction profile is large compared to the instrumental profile, the kind of case in which the PFSR method is most likely to be helpful.
PROFILE-FITTING-STRUCTURE-REFINEMENT
APPLIED WITH X-RAY POWDER DATA: P. E. Mackie
and R. A. Young, Georgia Institute of Technology,
Atlanta, Georgia 30332 USA.

The Profile-Fitting-Structure-Refinement
(PFSR) method has been applied with X-ray powder
data to several cases occurring in different
space groups. Previously applied to neutron
data by others (e.g. Rietveld 1969, Hewatt 1973,
Fender, et al. 1974), the method tends to utilize
all of the information present in a powder dif-
fraction pattern because it involves point-by-
point fitting, in a least-squares sense, of the
entire I vs 20 data set. The computer program
of Rietveld, modified by Hewatt and further mo-
dified for the X-ray case by Von Dreele and
Mackie, was used. It differs in details from
that of Lucas (1975). With a sharp pattern
(fluorapatite), fitting to 1868 data points led
to $R = 9.7\%$ based on 115 $|F|^2$'s with 28 para-
eters varied; of which 21 were atomic. Stan-
ard deviations in positional parameters were
$\pm 0.01\AA$ ($\sin \theta / \lambda < 0.42$).

Remarkably precise lattice parameters are ob-
tained as a spin-off benefit of the PFSR method.
In the sharp pattern mentioned, precisions of 3
parts in 100,000 were obtained (two parameters)
from data all below $2\theta = 77^\circ$. From the rather
"smeared" (FWHM $> 1.1^\circ$ at $2\theta = 31^\circ$) pattern of
a monoclinic material, 1 part in 2,000 for the
3 cell edges and $0.04^\circ$ for $\beta$ resulted.

PFSR fitting to the major phase in a multi-
phase mixture permits improved identification
and analysis of the minor phases by effective
stripping out of the major phases contribution
to the overall powder pattern.
EFFECT OF CHLORINE ION VACANCIES ON THE
LOCAL ATOMIC PARAMETERS IN NON-STOICHIOMETRIC
CHLORAPATITE, J.C. Elliott, London Hospital Medical
College, R.A. Young and P.E. Mackie, Georgia Institute
of Technology, Atlanta, and E. Dykes, London Hospital
Medical College.

Apatites are normally hexagonal with space group
P6_3/m, but stoichimetric (or nearly stoichimetric)
flux-grown chlorapatite, Ca_{10}(P0_4)_6Cl_2, is pseudo-
hexagonal with a doubled b axis and monoclinic space
group P2_1/b; this lowering of symmetry is associated
with an ordered arrangement within and between columns
of Cl ions in the structure (Mackie, Elliott and Young,
Acta Cryst. B23, 1840, 1972). On the other hand, melt-
grown chlorapatite has a deficiency of Cl which hinders
the propagation of the ordering information and
consequently prevents the formation of an ordered
structure so that the space group remains P6_3/m.

The structure of a 0.43 mm diameter melt-grown crystal
was determined from 1509 reflections measured with MoK
radiation (\( \lambda = 0.70926 \text{Å} \)). Lattice constants calculated
from 12 reflections were: a = 9.615 and c = 6.771Å with
\( \sigma = 0.002 \text{Å} \). These give a value for x of 0.10 in
Ca_{10-x}(P0_4)_6Cl_{2-x} using the lattice constant/chemical
composition relationships determined by Prener (J. Solid

The structure was refined by least squares followed by
Fourier difference maps which showed the presence of
satellites close to some of the principal atoms. These
were added to the structure and the process repeated
several times in order to find other satellites.
Satellites for Cl, Ca_{II}, Ca_{III}, and Ca_{I}(two) were found
with multipliers in the range 0.25 - 0.008. The final
weighted "reliability factor" based on \( F^2 \) was 4.2%. The
multipliers of the Cl indicated a loss of about 15%. 

82
It is thought that the first three satellites arise because they are adjacent to a Cl vacancy. These satellites are for Cl (displaced 0.857Å along the Cl column towards the mirror plane), Ca II (displaced 0.395Å towards the Cl column), and O III (displaced 0.369Å in a direction making an angle of 78.7° to the P-O III bond). The absence of detectable satellites for the other atoms in the PO₄ ion (O, O II, and P) is to be expected because they are more distant from the Cl vacancy. This is also consistent with the fact that the displacement of O III is accommodated by a distortion of a bond angle rather than a shift of the PO₄ ion as a whole.

The two Ca I satellites originate from Ca I ions adjacent to vacancies in the Ca I columns. These two satellites are displaced in opposite directions along the Ca I column by 0.315 and 0.313Å. The unexpected fact that there are vacancies in the Ca I columns shows that charge compensation for the loss of Cl requires the loss of Ca I (3Å from the Cl vacancy), as well as Ca II (adjacent to the Cl vacancy).

The magnitude of the multipliers of the satellites can give information about the clustering of Cl vacancies. Every Cl vacancy will cause a Ca II and O III satellite, but only those vacancies adjacent to a Cl ion can cause a Cl satellite. In fact, the multiplier of the Cl satellite is lower than would be expected for isolated Cl vacancies, so an appreciable amount of clustering is indicated.

This work was supported in part through NIH-NIDR Grant DE-01912 and the melt-grown crystal of chlorapatite kindly provided by Dr. P.D. Johnson.
STRUCTURAL FEATURES OF OXYPYROMORPHITE Pb_{10}(PO_{4})_{6}O,

K. Sudarsanan and R. A. Young, Georgia Institute of Technology, Atlanta, Georgia 30332.

The title compound, "lead oxyapatite", is expected to be structurally similar to calcium apatites, such as Ca_{10}(PO_{4})_{6}F_{2}, the Ca^{2+} being replaced by Pb^{2+} and 2F^- by O^{2-}. While the a axis, 9.823(2)Å and occurrence of trigonal-system symmetry (P6_{3}/m for fluorapatite) are in accord with expectation, the c axis is doubled (14.859(2) vs 6.884Å for fluorapatite). It was anticipated that the explanation of this doubling might be found in the ordering of the oxygen ions (Wondratschek, 1963) replacing F^-. Structure refinements with x-ray data from two small (<0.15mm) melt-grown crystals kindly supplied by Prof. H. Wondratschek were successful in P6. Except for the Pb(2) triangles and their associated oxygen ions, the atomic arrangement is similar to that in apatite. The Pb triangles in each "doubled" cell were found to occur in 3 distinct sizes, edge lengths being 4.376(2)Å at z = 0, 4.109(3)Å at z = 1/4 and 3/4 and 3.783(2)Å at z = 1/2. Oxygen ions were located at 0,0,1/2 in the center of the smallest Pb triangle and at 0,0,0.20 (and 0.80), near the intermediate size triangles, but not at 0,0,0 in the center of the largest Pb triangle. Oxygen site occupancy factors for these 3 locations were 0.64(14), 0.66(18) and 0.00(25), respectively. The size difference between the small and the large Pb triangles is consistent with the occurrence and non-occurrence of O ions at their centers. The intermediate Pb-triangle size may be occasioned by the associated O ion not lying in the plane or by a real difference in site occupancy factors here obscured by the large errors. This work has received financial support from NIH-NIDR Grant DE C1912

The interesting question was why the c axis was doubled, i.e. why and how the oxygens aggregated along the b axis instead of being equally spaced. "How" is at least partially answered; "why" is still a mystery.
Hydroxyapatite Variability Shown by Deuteration.
R.A. Young* and Derrold W. Holcomb. Georgia Institute of Technology, Atlanta, Georgia

Deuteration kinetics can be used as a probe to investigate differences among hydroxyapatite (OHAp) preparations. Aqueous preparations (by hydrolysis of CaHPO₄ or by precipitation) deuterate readily in a few hours at 110°C. High temperature preparations (conversion from chlorapatite at 1200°C) do not. The aqueous preparations show hexagonal crystal symmetry; the high temperature preparations are monoclinic. Degree of deuteration was assessed with intensity measurements of the infrared OH and OD stretch bands. The aqueous preparations, only, show a broad "water" IR band in the 3452-3550 cm⁻¹ region. It is strongly reduced and replaced by discrete peaks, at ~3540 cm⁻¹ and 3495 cm⁻¹, on heating of the specimen at 900°C for 5 hours. (No F nor Cl was present.) These observations suggest that much of the OH in the aqueous preparations is initially disordered, that on initial heating it tends to settle into more than one kind of site, and that the disorder may be related both to the occurrence of the hexagonal form and the ease of deuteration.

If diffusion controlled, as seems probable, deuterizability might be used as an indication of diffusibility of OH ions along the column, such as would be implicated in some models of the anisotropic acid dissolution of OHAp and, by extension, caries attack. Replacement of about 1 in 10 hydroxyl ions by fluorine ions, however, did not significantly reduce the deuterizability in the one case tried.

This work received support through NIH-NIDR Grant DE 01912.
Dielectric Properties of Ca₅(PO₄)₃Cl, "Chlorapatite". E. O. Rausch and R. A. Young, Georgia Institute of Technology—Nearly stoichiometric chlorapatite exhibits a dielectric constant > 10⁴, dielectric anisotropy > 10³, an apparent ferroelectric character, and time-dependent d.c. conductivity. At 1000 Hz and 25°C ε' > 10⁴ and ε'' > 10³ parallel to the c axis while < 10 and < 0.01, respectively, perpendicular to c. (Substitution of 4% of the Cl by F reduced ε' parallel to c by a factor of 100.) D vs E hysteresis loops (compensated) were observed even though the space group of the crystal is centrosymmetric (P2₁/b). At -200°C d.c. fields ≥ 1000 V/cm produced a d.c. conductivity (10⁻⁹ < σ < 10⁻⁶ mho/cm) which decayed within minutes to < 10⁻⁹ mho/cm in constant field. Dielectric measurements were made on single crystals in vacuum (to eliminate an otherwise debilitating adsorbed water problem) as functions of temperature (25-500°C), frequency (0-10 MHz) and composition. An ionic defect model accommodating all of the above phenomena involves (a) migration of Cl vacancies along the Cl chain (eₐ > -1 ev) and (b) small shifts (0.1 Å) of Cl ions adjacent to vacancies (eₐ < 0.2 ev) and of segments of the Cl ion chains along the chain direction. This work was supported in part by the USPHS through NIH-NIDR Grant DE-01912.
Control of Properties by Crystal Structural Details and Defects in Apatites.
R. A. YOUNG, Georgia Institute of Technology, Atlanta. (30 min.)

Properties considered in this work include unusual dielectric and diffusion properties, solubility, phase stabilization and change, fluorescence, thermal products, and accommodation of multiple and extensive substitutions. One theme in the work is that of large effects resulting from small differences. The apatites studied have ideal formula $A_5(MO_4)_3X$ where $A = Ca, Sr, Cd; M = P, As, V; and X = OH, F, Cl, CO_3, O, □$, and combinations thereof. Structural details determined include structural locations, roles and amounts present of minor and major ionic substitutions, interactions of $X$-ions, effects of various minor substitutions on location and bonding of the other ions, and ordering and defect mechanisms. Another theme of the work has been tension of the capabilities of the central technique, x-ray diffraction, and complementary use of others for the determination of the needed details. X-ray powder and single crystal diffraction techniques have been complemented with neutron diffraction and scattering, infrared spectroscopic, NMR, thermochemical and wet-chemical techniques. The individual study tasks were generally selected with a view toward furthering understanding of biological apatites, found in teeth and bone. With the base of information from synthetic and mineral apatites, the techniques have been exercised for the study of the natural biological material, human tooth enamel.

This work has been supported by the National Institute of Dental Research. I am grateful to many colleagues who have participated significantly in this work, and most particularly E. Mackie, K. Sudarsanan and J. C. Elliott.
THE STRUCTURES OF SOME CADMIUM 'APATITES'
$\text{Cd}_5(\text{VO}_4)_3\text{I}$, $\text{Cd}_5(\text{PO}_4)_3\text{Br}$, $\text{Cd}_5(\text{AsO}_4)_3\text{Br} \& \text{Cd}_5(\text{VO}_4)_3\text{Br}$.

K. SUDARSANAN and R. A. YOUNG, Georgia Institute of Technology, Atlanta, Georgia 30332, USA, and A.J.C. WILSON, Department of Physics, University of Birmingham, Birmingham B15 2TT, England.

All these cadmium apatites are more or less isostructural and the non-halogen atoms occupy much the same structural locations as in calcium apatites. But the halogen ions are too large to pack in the usual fashion at $\pm(0,0,1/4)$ on the sixfold axis of apatites; instead they occur in linear chains in which normal halogen-halogen distances obtain within the chains and the halogens do not occupy any unique position $\pm(0,0,z)$ on the hexad axis. The ionic diameters of the halogens exceed $\frac{3}{4}$c by as much as 10-20%. Relative to the oxygen atoms, they are present in less than stoichiometric amounts, the deficiency being 26% in the iodide case and 8% in the arsenate bromide case. The deficiency follows from the successive displacements of the halogens along the 6-fold axis and the occurrence of vacancies at the chain ends. Refinements of the crystal structures of the title compounds (final R's about 0.05) indicate that the formula should be written $\text{Cd}_{5-x}(\text{VO}_4)_3\text{X}_x$ where $x$ can be as large as 0.13 in one (the iodide) case.

We thank the National Institutes of Health (grant NIDR DE-01912), The Royal Society and the William Waldorf Astor Foundation for financial support.
DISTRIBUTION OF THE HALOGEN ATOMS IN FIVE CADMIUM 'APATITES', Cd₅(MO₄)₃X

A. J. C. WILSON, Department of Physics, University of Birmingham, Birmingham B15 2TT, England, and K. SUDARSANAN and R. A. YOUNG, School of Physics, Georgia Institute of Technology, Atlanta, Georgia 30332, USA.

The compounds are approximately isostructural with fluorapatite, but the halogen atoms are too large to pack in the ideal positions on the hexad axis. They (and Cd) are present in less than stoichiometric amounts, and are statistically distributed over a range of positions on either side of ±(001). Determination of the distribution has been attempted in three ways: (i) Fourier atomic-centre density syntheses, (ii) least-squares refinement of the occupancy of a multiplicity of sites uniformly spaced along the hexad axis, and (iii) fitting postulated distribution functions to the 'observed' structure factors corresponding to halogen centres only. All three methods are limited similarly by the resolving power afforded by the reflexions in the accessible volume of reciprocal space. The results are consistent with the 'chain' model postulated by Sudarsanan, Wilson and Young (Acta Cryst. A 28, S 151, 1972), the chain length ranging from about 3 atoms (M = V, X = I) to 8 atoms (M = As, X = Br).

We thank the National Institutes of Health (grant NIDR DE-01912), The Royal Society and the William Waldorf Astor Foundation for financial support.
A STRUCTURAL INTERACTION OF Cl AND Ca IN APATITES. R. A. Young and K. Sudarsanan, Georgia Institute of Technology, Atlanta, Georgia 30332

The "X-ions" (e.g. Cl, F, and OH) in calcium apatites (Ca$_5$(PO$_4$)$_3$X; P6$_3$/m) are coordinated by a triangular array of calcium, Ca(2), ions. In a composition series of 6 apatites with both Cl and other X ions present those Ca ions, Ca(23), coordinating Cl have been distinguished with single-crystal x-ray data from those, Ca(2A), coordinating F or OH and "superimposed" <0.2Å away. Although the a lattice parameter decreases as the Cl ion moves closer to it with decreasing Cl content [center-to-apex triangle dimension Δ=2.52Å & z=0.44 for X=95% Cl ranging to Δ=2.60 & z=0.36 for 70% Cl] while the Ca(2A) triangle changes little or none.

The correct distinction of Ca(2A) and Ca(2B) was verified by the correlation of (1) Cl site-occupancy with Ca(2B) site-occupancy (2) Cl z-parameter with Ca(2B) triangle size in a way that maintained normal 2.75(2)Å Ca-Cl distances and (3) the Ca(2) thermal parameter excess initially found [not distinguishing Ca(2A) and Ca(2B)] with the Ca(2B) site occupancy ultimately determined. Since the Cl position depends strongly on the amount of Cl present but very little on whether the other X ions are F or OH, prediction of the approximate z position for Cl simply on the basis of the amount present seems permissible.

We thank Dr. E. Kostiner, Dr. E.J. Young, and Dr. P. Cooray for specimens and the PHS for financial support through NIH-NIDR Grant DE-01912.

Key idea sentence:
The use of Cl content as a variable made it possible to sort out those Ca triangles associated with the Cl and to follow their changes correlated with Cl position changes.
EXPERIENCES WITH X-RAY PFSR: PROFILES, LaPO₄, AND TOOTH ENAMEL. P.E. Mackie, Dennis B. Wiles and R.A. Young, Georgia Institute of Technology, Atlanta, Georgia 30332.

PFSR, Pattern-fitting-structure-refinement, here designates the method developed by Rietveld (1969) for neutron powder data and adapted by R.B. von Dreesele and ourselves (ACA March 1975) for x-rays. It has now produced a number of new structural results, including the P and O positions in LaPO₄. PFSR of a number of materials both with Cauchy and with Gaussian profiles show that neither is close to optimum (as should be expected), the Gaussian function is the better for our diffractometer patterns with sharp profiles, and the wR_p-factors (whole-pattern, weighted) now running 10-30% will be substantially reduced by the selection and use of better profile functions. The PFSR program is being completely rewritten to, among other things, make easier the incorporation of different profile functions and other features as well as to improve its structure and portability.

The greatest single advantage of PFSR is probably, its potential for providing crystal structural information not otherwise obtainable about materials in their natural state, e.g. biological, botanical, some mineral, etc. A PFSR of human tooth enamel illustrates the point, providing for the first time structural details for this biological apatite. The principal atom positions are similar to those in synthetic hydroxyapatite but there are discrepancies reflecting substitutions. The substituting Cl appears to be at z = 0.33 in agreement with prediction (Young, Suckerman, this meeting).

Portions of this work were supported by NIDR Grant DE-04151 and other portions by NIDR Grant DE-01912.

Key idea sentence:
Crystal structural information (of materials in their natural state) was obtained by least-squares analysis of x-ray powder diffraction data.
Preliminary Crystal-Structure Analysis of Powdered Human Tooth Enamel. P.E. Mackie* and R.A. Young, Georgia Institute of Technology, Atlanta, Georgia 30332.

The Pattern-Fitting-Structure-Refinement x-ray diffraction method has been applied to powdered human tooth enamel to provide for the first time quantitative structure analysis of the crystalline portion of tooth enamel, per se. For this unheated dense (sp. g. > 2.95) tooth enamel with 1305 intensity observations $a=9.450(1)$Å, $c=6.892(1)$Å, and $R_p=25\%$ were obtained. Generally, the atomic locations are found to be similar to those expected but discrepancies do occur which reflect substitutions needing further analysis and specific incorporation in the model. Differences (>15σ) in the apparent positions of the phosphate oxygens may be due to carbonate substitution yet to be quantified by improved refinements. Scattering density is found distributed along the hexad axis in such a way as to accommodate F, Cl, and OH ions. At this stage, the possible occurrence of other entities, such as $\text{H}_2\text{O}$ in the hexad axis region is not conclusively assessed.

Pattern fitting with Gaussian profiles was found to be improved if for each reflection a profile corresponding to 100Å crystallite size was used in addition to the major profile corresponding to a several hundred Å crystallite size. Although it is known that a single Gaussian profile will not give the best possible fit, the possibility remains and is being carefully assessed that this result indicates a bi-modal distribution of crystallite sizes in human tooth enamel.

This work has been supported in part by NIH-NIDR Grant DE-04151.
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Quantity-Dependent Location of Cl in Apatites
K. Sudarsanan* and R. A. Young
Georgia Institute of Technology
Atlanta, Georgia 30332

The position of the Cl ion in (F,OH,Cl) Apatite depends on the amount of Cl present roughly similarly whether or not F is present approximately as z = z₀ - ax where x = 1 - y and y is the fractional amount of Cl present based on y = 1 for ClAp. a = 0.08 ± 0.02 and z₀ = 0.448. The Cl position is, presumably, changed in consequence of packing with OH and F along the X-ion column. As the Cl ions move closer to the associated Ca(2) triangle they expand such that the same Ca(2)-Cl distance (2.70(1) Å) is maintained. Of the total Ca(2) triangles, that fraction not associated with Cl does not change size significantly with variations in Cl content.

These results were obtained from 7 x-ray structure refinements for single crystals covering the range 0.1 < x < 0.95. Correlations of z(Cl) with Ca(2B) triangle size and of Cl site occupancy with Ca(2B) site occupancy corroborate the Cl-Ca(2B) interaction specified.

We thank Dr. E. Kostiner for the synthetic (Cl,OH) apatite crystal used, E.J. Young and P.G. Cooray for mineral specimens and the PHS for financial support through NIH-NIDR Grant DE-01912.
Dynamic Pyrolysis Studies of Human Tooth Enamel, R.A. Young*, Derrold W. Holcomb and P.E. Mackie, Georgia Institute of Technology, Atlanta, Georgia 30332

Human tooth enamel (TE) is being studied via the identity, amount, temperature and rate of evolution of its breakdown products produced by heating to >500°C. Several types of physical measurements are to be correlated. Thermogravimetric analysis (TGA) of the solids and infrared spectroscopic (IR) characterization and at-temperature monitoring of the evolved gaseous species have been carried out on the dense (sp.g.>2.95) portion of TE. The two major shoulders in the TGA curves (-40 to 120°C and >350°C) correlate reasonably well with IR evidence of strong evolution of H₂O in two temperature ranges (monitored at 3450cm⁻¹ as a continuous function of temperature). A light organic species (monitored at 967cm⁻¹) evolves strongly starting at 250-300°C, CO₂ (monitored at 232cm⁻¹) behaves similarly and H₂O starts strong evolution (its second) at a 30 to 40°C higher temperature. Off-line IR showed structural OH (3570cm⁻¹) increased by heating in this range. The sharpness of the second TGA shoulder is greater with larger particles, which appear to explode off pieces. A possible picture is of decomposition of protein and evolution of CO₂ followed or accompanied by explosions of pockets of trapped gases and strong evolution of H₂O, all in the range 350-450°C. Whether the pockets initially contain the "trapped water" reported from NMR measurements (e.g. Myers 1965) is not yet determined.

This work has been supported in part by NIDR Grants DE-04151 and DE-01912.

SUMMARY

In the preceding application, work was proposed in four areas: (I) development, in atomic scale detail, of structural components of a realistic model for TE (tooth enamel mineral), (II) assessment of the extent and condition of occurrence in TE of the various model elements, (III) application of results to understanding processes in TE, especially diffusion processes, and (IV) development and acquisition of special study tools needed. Progress has been made in each of these areas. In several cases the progress to be reported relates simultaneously to two or more areas. Eleven full papers (two of them, P8 and P10, quite major) reporting the results were submitted for publication during this period. Seven contributed papers and three major invited papers on project work were presented at scientific meetings. The principal accomplishments constitute substantial advances (1) with respect to understanding based on the direct study of the atomic arrangements and processes in TE, per se, especially with respect to structurally incorporated \( \text{H}_2\text{O} \) and \( \text{CO}_3 \) locations and evolution processes, (2) with respect to factors affecting the \( \text{OH} \) diffusion processes and, in turn, solubility of TE and apatites, (3) with respect to atomic arrangements in related, potential model, materials, and (4) with respect to the improvement of methodologies for studying these important atomic-scale phenomena.

The crystal structure of TE per se was refined for the first time, in this case an initial refinement on a modified hydroxyapatite model. Though there are many similarities to OHAp, there is also a number of very significance differences.

The \( \approx 4 \) wt% water in TE was shown to be structurally incorporated, to be definitely associated with the a lattice-parameter expansion of TE (cf. OHAp) as previously suggested by LeGeros, Bonel & Legros (1978), to be distinguishable from adsorbed water even in i.r. spectra (when made with a really good unit), and probably to be located in the X-ion channels in limited orientational disorder approximately about 0,0,0.12 [P6 & P8].

The 3-4 wt% \( \text{CO}_3 \) present in TE was shown to start evolving at temperature as low as 100°C. This is an unexpected result which might have clinical implications. Greatly increased importance has been attached to A-site \( \text{CO}_3^- \) in TE. Not only is it present in larger amounts (15-20% of total present) than previously thought, but the A and B sites are interconnected; on thermal evolution, much of the B-site \( \text{CO}_3 \) passes through A sites on the way out of the TE crystals [P8]. (Thus, the distribution of \( \text{CO}_3^- \) between A and B sites must be the consequence of dynamic chemical equilibration at 37°C.) A detailed structural location for A-\( \text{CO}_3^- \) has been specified in synthetic preparations [P10] and tentatively found also in TE [A7]. Fully carbonated synthetic apatite exhibits ordering of the \( \text{CO}_3 \) groups in two ways and has space group Pb (cf. \( \text{P6}_3/m \) [P14].

Acid solubility ($K_{sp}$ or kinetics, or both) of variously prepared OHAp and, by inference, TE appears to correlate with OH diffusibility along the X-ion channels [P11]. Possible mechanisms for the diffusion and for its enhancement or inhibition by various agents or conditions are beginning to emerge and may lead to some general rules with predictive value. Such rules could be a major contribution to the understanding of solubility differences and how to control them and, hence, cariogenicity. Vacancies, disorder, and both steric and bonding effects of various substitutions are key factors.

Some properties of "pure" synthetic hydroxyapatite have been shown systematically to vary, sometimes greatly, with preparation method, e.g., precipitated, refluxed, hydrothermal, or prepared at 1000°C in steam from Ca$_2$P$_2$O$_7$+ CaO. The accumulating evidence is that these differences are caused by differences in OH site filling (vacancies), OH ordering, and incorporation of H$_2$O [P11, A8, & in preparation].

Some important atomic-arrangement details have been studied for the first time in several potential model systems, which are particularly relevant to TE in part just because they are polycrystalline, as is TE. These materials include several differing preparations of OHAp, some oxy- or oxy-hydroxyapatite, A-type carbonated apatite [P10], and thermal products of some of the OHAp's and, especially, of TE. Most of these materials could not be made available as single crystals either (1) at all or (2) without possible, or certain, distortion of some of the atomic-scale features of interest. There are marked differences among these materials in the occupation of the X-ion channels of the apatitic phase. Both distribution and amount of the occupation differ. It is the Rietveld method (of whole pattern fitting crystal structure refinement with powder diffraction data) that, uniquely, has made these determinations possible.

More than 200 Rietveld-method structure refinements of TE and apatites have been carried out. (a) Their accumulated results constitute a very useful data base now being computerized. (b) From this extensive experience with the Rietveld method, many valuable things have been learned about the method's strengths and weaknesses, about what it can and cannot do, and about the reliability of the results [P5, P7].

A much-improved computer program for the Rietveld method has been written [P15]. It is more powerful, is more convenient to use and to modify, provides higher throughput, and is more verifiably correct than the earlier-used modification of a program initially written elsewhere and for the neutron case only. Because of the importance of the Rietveld method to our work, and because of the size of the program required (in excess of 5500 FORTRAN statements), completing this new program and bringing it into our daily service does constitute a major accomplishment; doing the same for a lesser and less-important program would not.

The floating-point processor has been installed in the PDP8E computer controlling the single crystal diffractometer and the data-collection routine has been re-written in FORTRAN so that it can be used and modified with reasonable ease by various users. (It was previously in assembler language.)

Acquiring and putting into regular service the new IR instrument (PE 580B) has had a very positive impact on the project in many ways, e.g., throughput, data quality, data type, and experiment control.
Thanks to the Rietveld method, to the very good i.r. instrument in our own lab and to the background of structural information about related materials that has been built up, we are more and more able to address our efforts directly to TE, per se.

FURTHER DETAILS

1. The Rietveld method of doing crystal structure refinements from powder diffraction data has been used extensively (more than 200 different refinement runs) to study TE in itself and in comparison to synthetic hydroxyapatite [A9, A8]. Some real insight into atomic detail of TE has been obtained and it is now clear that still more can be obtained with this method.

   a. Crystal structure refinements of human tooth enamel (the first ever) have been carried out on a modified hydroxyapatite model without the as-yet-unlocated HPO$_4^{2-}$ and B-CO$_3^{2-}$ groups known to be present [P6].

   b. There are significant differences between untreated TE, (dense fraction i.e., sp.g.>2.95), and synthetic hydroxyapatite (OHAp) refined on the same model.

   (1) The total scattering density $\Sigma n(X)$ from the X-ion channels ($X = \text{OH, F, Cl, \ldots}$) is $\geq 2$ times that expected and observed for stoichiometric OHAp.

   (2) A structural location has been put forward for the H$_2$O structurally incorporated in TE. Differences between x-ray and neutron Rietveld refinement results are consonant with the excess $\Sigma n(X)$ being largely H$_2$O in some orientation disorder and centered near 0,0,0.12. The amount of the excess $\Sigma n(X)$ if ascribed to H$_2$O is consonant with the $\sim 4$ wt% H$_2$O found in TE [P6].

   (3) Differences of 0.1 to 0.2 Å in apparent positions of two of the phosphate oxygens, and in the apparent site occupancies for two of them, give promise that the actual structural positions of the CO$_3^{2-}$ in the B sites (presumably replacing PO$_4^{3-}$) in TE can eventually be directly determined.

   (4) The causes of the expansion of the a axis ($\sim 0.02$ cf. reference OHAp) are not the same for TE and for OHAp prepared by a reflux method; the excess in $\Sigma n(X)$ correlates positively with a expansion in TE but negatively in reflux OHAp. (Both TE and reflux OHAp lose this a expansion on being heated to $<400^\circ$C.) This is consonant with the a expansion in TE being due to H$_2$O in the X-ion channels.

2. X-ray, neutron, i.r. and other studies of the products of heating of TE and OHAp under various regimens have led to many new results.
a. Further differences, in structural detail, between TE and OHAp resulting from heating were shown by comparative x-ray Rietveld analyses (work in progress).

(1) The differences are consonant with the causes of the a axis expansion, which is removed by heating to 400°C, being H$_2$O in the X-ion channels in TE but not in reflux OHAp.

(2) The OH$^-$ in TE is at a somewhat different position than in OHAp ($z = 0.12 - 0.13$ vs 0.19). The cause of this difference may well be significant to the functioning of TE, but the cause has not yet been determined.

b. Marked loss of structural H$_2$O from TE heated to near 300°C correlates well with the loss of the a axis expansion, and thus gives support to LeGeros' suggestion (LeGeros, Bonel and Legros, 1978) that H$_2$O is responsible for the expansion [P8].

c. The thermal coefficient of expansion of TE that has never been heated above ~270°C is (a) larger than that of TE heated to higher temperatures and (b) increases with temperature, thus indicating increasing disorder just prior to the a axis contraction [P8]. Once the contraction temperature has been exceeded, or at least once the TE has been heated to 500°C, the thermal coefficient of expansion stabilizes at ~11x10$^{-6}$/°C.

d. Some thermally induced changes in TE take place at such low temperatures that they may have direct relevance to clinical dentistry [P8]. For example, they might occur at the surface of a TE site being prepared in vivo for restoration.

(1) CO$_3^{2-}$ is lost, from both A and B sites, in TE at temperatures as low as 100°C.

(2) The decrease in A-CO$_3^{2-}$ (that in the channels) in TE up to about 400°C is accompanied by an increase in structural OH, which suggests the reaction H$_2$O + CO$_3^{2-}$ $\rightarrow$ 2(OH)$^-$ + CO$_2$ (diffuses out).

(3) Because grinding is such a forcible process, tearing apart particles and breaking bonds, it is possible that the effective temperature in the outer atomic layers of TE being ground, even under a water jet, may reach temperatures high enough to promote the material changes in a & b, above.

e. Much or all of the CO$_3^{2-}$ in B sites (probably in phosphate positions) in TE passes through A sites (in the X-ion channels) on the way out of the crystals. A CO$_2$ intermediary is involved [P8]. Thus, the relative importance of A-CO$_3^{2-}$ in TE is greater than its fractional occurrence, ~15% of the CO$_3^{2-}$ present, would suggest.

f. A-CO$_3^{2-}$ in untreated TE is the same as that in high temperature preparations of carbonated apatite and TE [P10]. Above 400°C, A-CO$_3^{2-}$ (having previously diminished) builds up in thermally decomposing TE until it
reaches a maximum at ~800°C. The i.r. bands do not shift by even one wavenumber, showing that the environment of the CO$_3^{2-}$ is the same throughout. The amount is $\sim$ twice that initially present. It is responsible for the previously reported (e.g., LeGeros, Trautz, LeGeros and Klein, 1970) 0.02-0.03 Å 800°C expansion of $a$ and for $\sim$30% increase in the x-ray scattering from the X-ion channels. Rietveld analyses showed the A-CO$_3^{2-}$ to be present at a location similar to that in TE and apatite deliberately carbonated at 100°C in dry CO$_2$. Thus, the i.r. indication of similarity of A-CO$_3^{2-}$ in untreated TE to that in high temperature preparations is corroborated.

3. Long-sought new results have been obtained for A-type CO$_3^{2-}$-apatite, which permitted completion of papers P10 & P14.

a. Completely reversible CO$_3^{2-}$ $\leftrightarrow$ 2(OH)$^-$ exchange was demonstrated in both OHAp and TE. The specimens were heated at 1000°C, first in a specially dried CO$_2$ stream and then in H$_2$O vapor, or vice versa [P10]. Parallel experiments were carried out with human tooth enamel (fraction with sp.g.$>$2.95) and synthetic OHAp and with the complementary use of x-ray diffraction, neutron diffraction, infrared spectroscopy, and thermochemical techniques. This particular study constitutes a major effort extending over more than eight years and involved collaboration with the Toulouse group. Significant points are that this exchange does take place, that it is reversible, that it occurs in TE (or, rather, the pyrolysis product of TE!), and that when full carbonation is approached the least traces of H$_2$O in the CO$_2$ stream are taken up preferentially. Yet the first stages of carbonation go easily. Thus, the occurrence of CO$_3^{2-}$ substituting as a minor fraction, but only a minor fraction, of the OH sites in TE is in accord with the implications about chemical balance arising from these experiments.

b. A-site CO$_3^{2-}$ was located (by Rietveld analysis) in the X-ion channel with C near 0,0,0.12 and the CO$_3$ plane making an angle of $\sim$18° with c. In the incompletely carbonated specimens so studied, the CO$_3$ groups occupied statistically the 6 nearly equivalent positions with C at this point and the average space group was, then, still P6$_3$/m [P10].

c. In nearly fully carbonated apatite (e.g., $>$85%) this disorder in the CO$_3^{2-}$ position is removed and the crystal symmetry changes to the monoclinic space-group Pb [P14]. It does, however, remain pseudo-hexagonal with b = 2a and $\gamma$ differing from 120° only by 0.36°. At first thought, the physical structure seems rather parallel to that in monoclinic hydroxyapatite and chlorapatite. But it is much complicated because the CO$_3^{2-}$ group is ordered in two ways, both in the sense of above vs below the mirror (now glide) plane and in the sense of rotation about the c-axis.
axis. A screw axis occurs in both hexagonal (63) and monoclinic (21) hydroxyapatite and chlorapatite parallel to c but no rotational symmetry exists in this new phase. There is some evidence that these two types of order are lost, on heating, at different temperatures.

Although it had been known for years that the space group changed on full carbonation (e.g., the 00.1 reflection appeared in neutron diffraction patterns of the carbonated materials [P10]), the ordering subtleties made the determination of the new space group unusually difficult. (Single crystals, of course, were not available.) It was finally done in an international cooperative effort involving persons and equipment in Toulouse, London and Atlanta [P14]. Rietveld analyses of this ordered material may provide improved definition of the A-CO3\(^{-}\) location.

4. A part of the ongoing program is to determine the structural locations and roles of "substitutions", by which we really mean atomic population differences in TE and ideal OHAp.

a. One of particular interest is Sr for Ca because it is cariostatic and because radioactive \(^{90}\)Sr from fall out can be readily taken up in, yet eluted preferentially from, bone. The structural features of varying amounts of Sr-for-Ca substitution were studied with x-ray single crystal techniques. Sr was found to substitute preferentially for Ca(2) and to affect the position of Cl in (Ca, Sr) chlorapatite [P9]. Can these small features be the origin of the cariostatic effect? The first Sr, by substituting for Ca(2), does border the X-ion channels along which diffusion important to solubility is thought to take place [P11]. Since the Sr\(^{2+}\) ion size is larger than the Ca\(^{2+}\) size (1.92 vs 1.74 Å), it is possible that this Sr\(^{2+}\) may provide some steric hindrance to OH diffusion and, hence, some reduction of solubility kinetics, even if not Ksp. The displacement toward \(z = \frac{1}{2}\) of a Cl\(^{-}\) adjacent to an Sr\(^{2+}\) supports this idea, that a Ca(2) triangle with Sr substituted at one or more position has less openness and therefore it is harder for OH\(^{-}\) to get through.

If it should turn out that that is the mechanism, then it follows that a prescription for reduction of caries would be replacement of (some) Ca\(^{2+}\)(2) ions in TE with larger ones, e.g., Sr\(^{2+}\) & Ba\(^{2+}\). In contrast, smaller ions such as Mg\(^{2+}\) and Be\(^{2+}\) would be expected to be associated with an increased incidence of caries or severity of carious attack, just as has been reported to be the case for Mg\(^{2+}\) (Kigoshi, 1971; Halworth, et al, 1972).

b. Efforts have been made to grow a variety of single crystals for precision x-ray structure refinement studies of minor substitutions. We have concentrated on those substitutions which are most abundant in TE or are of special interest for other reasons. Our growth is from the flux (cooling slowly from \(\approx 1200^\circ\)C) with \(X = F^-\) or Cl\(^-\). Most of the metallic substituents of interest seem to have rather limited solubility in calcium chlorapatite. Only in the case of Sr have we gotten as much in as we would like. Table C-1 shows our recent crystal growth results.
### TABLE C-1

Doped chlorapatite crystal growth results

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<th>Prep'n.</th>
<th>Dopant, M</th>
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<th>Comments</th>
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<td>.5 50</td>
<td>&quot; &quot; &quot; &quot;</td>
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<tr>
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5. Hydroxyapatite variability

As a few workers were aware ten years ago (e.g., Bonel, 1970) and as is now becoming general knowledge, truly stoichiometric hydroxyapatite is not easily synthesized. The product does vary with the preparation method. Precipitated products, in particular, are highly sensitive to preparation details (e.g., Meyers, 1979; Moreno, Gregory & Brown, 1968; Bell, Mika and Kruger, 1978; McDowell, Gregory & Brown 1977; Mika, Bell and Kruger, 1976) and are significantly OH⁻ deficient (Bonel, 1972; Myers, 1979). Since OHAp is often used as a model, a starting point, a reference material, this variability makes problems. It has often compromised experiments reported by workers unaware that one "hydroxyapatite" may be very different from another.

We are trying to help this situation, for ourselves as well as others, by quantifying some of the differences among "OHAp" specimens prepared several different ways. The general methods of preparation are precipitation, reflux, hydrothermal, and high temperature conversion from ClAp and from Ca₃(PO₄)₂ made from Ca₂P₂O₇ and CaO. Other variables are heating temperature and atmosphere. The principal tests for differences are Rietveld analyses, i.r., spectroscopy, and deuterizability.

Significant differences are shown up by each method. X-ray analyses (Rietveld) show that lattice parameters, total content of the X-ion channels and crystalline phase differ. The i.r. analyses show that OH⁻ content and disorder differ. Deuterizability studies show great differences in the diffusibility of OH⁻. Some of the preliminary results were communicated in paper P11. A full paper on the subject of OHAp variability is in preparation. These results indicate that OH⁻ diffusion is enhanced by things which increase the availability of passing sites for the diffusing species in the X-ion channels (e.g., vacancies and disorder) and is inhibited by things which decrease that availability (e.g., all X-ion sites filled, fully ordered) or provide local pinning (e.g., H bonding to F⁻).
3. PUBLICATIONS PRODUCED DURING REPORTING PERIOD (21 May 1977 - 30 April 1980)

(a) Full papers published or submitted since last comprehensive report

P1.* "The Structure of Some Cadmium 'Apatites' Cd$_5$(MO$_4$)$_3$X. I. Determination of the Structures of Cd$_5$(VO$_4$)$_3$I, Cd$_5$(PO$_4$)$_3$Br, Cd$_5$(AsO$_4$)$_3$Br and Cd$_5$(VO$_4$)$_3$Br", K. Sudarsanan, R.A. Young and A.J.C. Wilson


(b) Published abstracts of presentations at scientific meetings.
[copies are included in Appendix]


(c) Other

In addition, three major project-based invited papers were presented for which the printed abstracts were not published in a journal but were only disseminated, primarily, to the meeting attendees. Each was also prepared as a full written paper, papers 5, 7, & 11 in the above list of full papers.
Tooth Enamel Apatite at the Atomic Level

1. List publications: (a) published and not previously reported; (b) in press. Provide five reprints if not previously submitted.

2. List all additions and deletions in professional personnel and any changes in effort.

3. Progress Report. (See Instructions)

1. Publications
   a) Published since last report
      (i) Full papers

      (ii) Abstracts
Publications (continued)


b) Submitted since last Report but not yet published
(1) Full papers


2. Additions and Deletions in Professional Personnel

None.
3. **Summary Progress Report**

Progress has been made in direct analysis of the crystal structural atomic arrangements in untreated human tooth enamel, (TE) in the methodology for carrying out such heretofore impossible analyses, in understanding of the "substituents" in TE by detailed pyrolysis studies with several complementary techniques, in the crystallographic aspects of Sr substituting in minor amounts for Ca in apatite, and in other areas.

The accomplishment that currently appears most significance is the first crystal structure refinement of human tooth enamel, per se. This was accomplished with Rietveld (whole pattern-fitting-structure-refinement) analyses of diffraction data from powdered TE (dense portion). Although stated to be "preliminary", the current results do locate the principal atomic species and give some information about possible substitutions in the apatitic "channels" wherein OH, F, Cl, some CO₃ and, possibly, the structurally incorporated H₂O in TE reside. The current stage of results is substantially beyond that reported in abstract 15 attached to the last report. Several tens of refinements have now been done with several different samples of TE and with improved computer programs and improved understanding of errors. Work on these crystal structure studies of TE and on the computer program involved has absorbed a very substantial fraction of our efforts since the last report.

The importance of this accomplishment lies both in the results, per se, and in the fact that it was possible to obtain them at all. The latter results from a triumph of technique (Rietveld analysis) which has made possible meaningful crystal structure refinements of materials, such as TE, that are simply not available in single crystal form. It is now a reasonable expectation that with continued improvements, such as we are working on, in the
technique and its application, it will be possible to locate the CO$_3$ and HPO$_4$, as well as H$_2$O, in normal TE. One suggestion for H$_2$O has already developed.

Structure refinements (i.e. adjusting parameters in a model to give the best least-squares fit between observed and calculated diffraction intensities) were done both with x-ray powder diffraction data and with neutron powder diffraction data. Because x-rays and neutrons are scattered differently, the results are complementary and, in this case, led to the suggestion that the structurally incorporated H$_2$O in TE in the amount of 1 to 2 molecules per unit cell is located in the aforementioned channels about midway between sets of Ca atoms ("Ca triangles") surrounding the channel. Additional refinements on heated specimens with x-ray data alone have been unable to confirm or deny this suggestion, probably because -- as we concurrently found from our i.r. studies, see below -- when TE is heated to 600-800° substantial amounts of CO$_3$ move into the channels, and thus can replace the x-ray scattering density lost with the departing H$_2$O. Since H$_2$O and CO$_3$ scatter neutrons very differently (the scattering length is negative for H and positive for the C and O), we will soon collect neutron data on a heated specimen and look to the structure refinement based on those data for the confirmation or denial of the suggested H$_2$O location.

The writing of the new computer program for doing Rietveld analyses, mentioned in the last report as being under-way, is now completed in Version II form. The design and writing of the new program turned out to be a major undertaking (more than FORTRAN statements) but it is now giving good service. It was used for all of the most recent refinements of TE. It has several advantages over the previously used program (a local adaptation, for x-rays, of the program written by Rietveld for the neutron case), such as our greater assurance of its internal correctness in detail (in part because
of its modular construction), specifically suited to the x-ray case, convenient single pass operation, and much easier modification. We will report on it at the next ACA meeting (See "Publications - Abstracts").

Important experience with the Rietveld method has been and is being gained which enables us to apply the method more effectively to recognize and avoid overstepping some of its limitations and to recognize directions in which further improvements can be made. At this point we have carried out more than 100 Rietveld-type structure refinements with a variety of specimens and models of TE and apatites with and without substitutions. We have used mostly x-ray data but also several sets of neutron data. We were invited to present, and have in press (see "Publications"), one paper on the subject, we will present another, on "False and Flat Minima..." at the March ACA meeting, and will give two more invited papers on the general subject next summer. Presently, precision in atom positions is about one order of magnitude poorer than that in good single crystal analyses (e.g. 0.01 Å instead of 0.001 Å), individual temperature factors have rarely been successfully refined, refined atom-site occupancies generally have standard deviations of at least several per cent, and the actual errors in the refined parameters seems to exceed the calculated standard deviations by a factor of 2,3, or more. It is clear that the most pressing improvement needed, to improve the structural detail obtainable, is better x-ray reflection profile functions. In part, the new computer program was written to accommodate the search for them.

The floating point processor for our PDP8E computer controlling single crystal x-ray diffractometer has been installed. We are now well along with the re-programming effort and now have in operation a control program written in FORTRAN. (The capability for effectively using a high level language, such as FORTRAN, was one of the reasons for adding the processor.)
New information about atomic/molecular scale make up of untreated TE is being determined from the changes that occur on heating (pyrolysis). Temperatures as low as 200°C, and perhaps 100°C, produce some irreversible changes, which fact may have implications for the selection and use of adhesive restorative materials, especially if the site is prepared by grinding (even though water is used for cooling). Changes now observed and not previously realized to occur at such a low temperature or not realized to occur at all are (1) generation and entrapment of CO₂ in the specimen following breakdown of CO₃ in both A and B sites or in sites indistinguishable from them on the basis of high quality i.r. spectra, (2) increase of the OH-stretch i.r. band intensity at 3572 cm⁻¹, indicating an increase in the structurally ordered OH, and (3) increase in the crystallographic a axis observed at temperature and "corrected" to room temperature.

On further heating the a axis increases up to about 250°C, where it abruptly decreases by ~0.02 Å. There is nothing in the TGA curve in this range to indicate a sudden loss of any mass, so we must assume that the decrease is caused by a re-ordering, e.g. with the expulsion of vacancies rather than by a sudden loss of any component. If so, this along with the OH 3572 cm⁻¹ behavior constitutes further evidence of the initially disordered state of the hexad axis region in TE.

On still further heating, the CO₃ in the B sites (which is where >90% of the CO₃ in TE is) continues to break down, more CO₂ is generated (2340 cm⁻¹) some of which becomes oriented (2200 cm⁻¹, polarized i.r. work done by J.C. Elliott, priv. comm.) along c, suggesting it has migrated to the hexad axis region, and CO₃ develops in A sites (the ones for which CO₃ replaces 2(OH)) to a maximum at about 800°C, at which temperature the expansion of the a axis suggests that about 20% of the CO₃ A sites are filled. This phenomenon
of apparent migration, first of CO$_3$ from B sites to A sites (first suggested by Emerson & Fisher, 1962, & now seen to be via 2 CO$_2$ intermediaries) opens the possibility that the A site and B site CO$_3$ in TE may not be entirely independent, a point of possible interest in the cariogenic effect of CO$_3$.

The role of Cl in TE is one of our project subjects. In the pyrolysis studies some account of Cl can be kept with the i.r. band at 3495 cm$^{-1}$ arising from OH-stretch perturbed by hydrogen bonding to an adjacent Cl. The 3495 cm$^{-1}$ band shows the same sort of increase and then decrease with temperature as does the 3572 cm$^{-1}$ (unperturbed OH stretch) up to about 800°C -- and even higher (both going to zero) if the ambient is free of water vapor. Since there is no opportunity for the Cl content to be increased with heating, the correlation of initial increases indicates that the ordering of the OH, or its generation in the hexad axis region, is little affected by the presence of Cl.

The Cl does seem to have an inhibiting effect on OH diffusion in the "channels" of the apatite structure in both TE and synthetic preparations. Deuterization-kinetics studies show that during the first several hundred hours the OD-OH exchange rate for OH hydrogen bonded to Cl is <70% of that for OH not so bonded (synthetic preparation).

The new i.r. instrument and having it in our own laboratory are great helps in these pyrolysis studies. We are able to get better spectra (more revealing, more quantitative, more reliable), to run many more spectra in a day, to better assess and control experimental-instrumental variables, and to fit the instrument with special apparatus such as our cell for studying the evolved gases.
Single crystal structure refinements of (Ca, Sr) apatite specimens grown here showed that Sr preferentially replaces Ca(2) rather than Ca(1). For 1 to 6 atomic % Sr for Ca, the Sr replaced only Ca(2). That is the Ca on the mirror plane and adjacent to the hexad axis channel. Sr substituting for Ca(2) does so at a slightly different (∼0.2 Å) location, which correlates with the ∼10% larger in size and, because of consequent lattice strains, with the slight preferential loss of Sr that has become incorporated in bone (e.g. Lengemans, 1957). Why the Sr should have a cariostatic effect (Curzon, Adkins, Bibby & Losee, 1970) is not clear. It may be related to the combination of the larger Sr ion size plus its preferential location at a site bordering the easy diffusion ion channel, thus somewhat inhibiting the diffusion of OH and other ions along these channels in TE.

Efforts were continued to prepare, for x-ray study, single crystals with cation substitutions present in TE. Single crystals have been grown of calcium chlorapatite with trace amounts (e.g. of the order of 1 wt%) of, variously, Li, Cu, Mn, and Cd. These efforts are being continued with the goal of increasing the substitution levels to ones more convenient for x-ray study.

There was, as usual, a miscellany of small things done, including a little more progress on the paper on \( \mathrm{CO}_3^{2-} \leftrightarrow 2(\mathrm{OH}) \) in apatite and "TE" at high temperature, all of which contribute to ongoing work that will be reported on when it is farther along.

Specific Goals for the Next Project Year.

Considerably more work remains to be done with developing the program, techniques, and applications methodology for the Rietveld analysis method. One immediate goal is to finish Version III of our new computer program, which will
have a multi-phase capability and some other advantages. This will be very useful for analysis of pyrolysis products wherein $\beta$-Ca$_3$(PO$_4$)$_2$ commonly occurs as a second phase. The next goal is to search out or develop, and to incorporate in our program, better reflection profile functions, the use of which will allow determination of more crystal structural detail from powder patterns.

Structure refinements of TE will be continued as opportunity for improvement occurs. For example, our refinements with neutron data resulted in $R_p \approx 29\%$ whereas the common experience of others with other materials is that $R_p$ falls in the range 7-10\%. Thus, with more extensive neutron data we may hope to refine on such things as CO$_3$ and, perhaps, HPO$_4$, which are not in our currently used refinement model of TE. As another example, when we get improved profile functions for the x-ray case it will be worthwhile to attempt refinement of a model containing more detail, e.g. CO$_3$.

A particular immediate interest is the confirmation or denial of the occurrence of H$_2$O as suggested from the neutron vs x-ray TE crystal structure results in hand. This will be attempted with a set of neutron data that we hope to get collected next month on TE that has been heated to 800°C. We already have the x-ray structure refinement for this material. It is hoped that comparisons of the results of the four sets of refinements, x-ray and neutron for both untreated and 800°C TE, will permit a definitive answer.

The pyrolysis work will be continued to obtain more reliable data (more precision resulting from repeated experiments). It will also be extended to smaller temperature steps so that better correlations can be obtained among the various things occurring, thus permitting us to distinguish cause and effect. In addition to temperature, kinetics and environment (e.g. vacuum, air, dry N$_2$ etc) are variables. Finally, there is the matter of TE specimen variability and the comparison of TE behavior to that of related apatites.
Another goal for the coming period is to complete single crystal structure analysis of CaCl$_2$-deficient chlorapatite and to undertake it on Ca(OH)$_2$ deficient hydroxyapatite. The latter will require the conversion of a single crystal of CaCl$_2$-deficient chlorapatite to a Ca(OH)$_2$-deficient single crystal of hydroxyapatite. We have previously converted single crystals of chlorapatite to single crystals of hydroxyapatite, but we do not know if the crystal will retain the deficiency during conversion.

Finally, another goal for the coming period is to finish off and submit for publication some of the many papers in various stages of completion, some but not all of which require small amounts of additional laboratory work.

The undersigned agrees to accept responsibility for the scientific and technical conduct of the project and of provision of required progress reports if a grant is awarded as the result of this application.

23 February 1979

Date

Principal Investigator or Program Director
SECTION IV

SECTION IV—SUMMARY PROGRESS REPORT

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Last, First, Initial)
Young, R. A.

NAME OF ORGANIZATION
Georgia Institute of Technology

PERIOD COVERED BY THIS REPORT
FROM 1 May 1980 THROUGH 30 April 1981

DE-01912

1. List publications: (a) published and not previously reported; (b) in press. Provide five reprints if not previously submitted.

2. List all additions and deletions in professional personnel and any changes in effort.

3. Progress Report. (See Instructions)

1. Publications
   (a) Published or put in press since last report

   i) Full papers (1-4 are in refereed journals):


   ii) Abstracts (listed primarily for convenience of reference in the Summary Progress Report)


2. Additions and Deletions in Personnel

Dr. K. Sudarsanan left Georgia Tech at the end of October 1979.

Dr. P. E. Mackie took over Dr. Sudarsanan's role temporarily while completing the training of others (J. R. Cagle and D. B. Wiles) to continue it.
3. **Summary Progress Report**

1. **Objectives**

   The overall objective of the project is to determine the atomistic mechanisms of the roles and effects of the various atomic and molecular species present, or that can be made to be present, in the mineral component of human tooth enamel (TE). Understanding mechanisms of beneficiation or detriment, of health and disease, in atomistic detail provides a necessary base upon which atomic-level modification can then, later, be made to adjust, or compensate for, the properties of tooth enamel in desired ways.

   The specific goals for the current year, as set forth in last year's summary progress report, included:

   1) Further development of the computer program, techniques, and applications methodology for the Rietveld analysis method, the powerful new method of extracting from powder x-ray and neutron diffraction patterns much more and better crystal structural information than heretofore.

   2) Structure refinements, with the Rietveld method, were to be continued on a variety of TE specimens, variously treated. Particular aims were to work toward eventually locating the HPO$_4^-$, the structurally incorporated H$_2$O, and the CO$_3$ in both A and B sites.

   3) The pyrolysis work with TE was to be continued to provide more reliable data (better known precision by virtue of repetition of experiments) and to use ever smaller temperature intervals to permit identification of cause and effect relationships among the various things going on during the thermal decomposition of TE.

   4) Comparisons were to be made of TE behavior to that of related apatite. The matter of TE variability was recognized as a possible factor needing exploration.
5) A single crystal structure analysis was to be made of a chlorapatite single crystal made CaCl$_2$ deficient by being heated in vacuum. Then that crystal was to be converted, if possible, to a Ca(OH)$_2$-deficient single crystal of hydroxyapatite (OHAp) and its structure was to be analyzed with x-ray diffraction methods.

6) A particular goal was to finish off and to submit for publication a number of the many papers in various stages of completion, some of which had been in progress for a very long time but needed small amounts of still more laboratory work and, in one case, collaborative effort. As the preceding list of publications shows, much of this goal has been achieved. Papers 3 and 4 in the list have particularly long work histories and are large papers reporting substantial accomplishments.

2. Results

The reporting of results here is representative but not comprehensive. Comprehensive reporting of some of the results is given in the publications listed on p.5.

Substantial progress has been made toward all of the goals listed above except (5). The work toward goal (5) has proceeded more slowly than expected. The slowness occurred in part because the single crystal diffractometer has been out of service a lot with hardware problems and new software development, and in part because the first CaCl$_2$-deficient single crystal examined proved not to have a large enough deficiency for reliable analysis. We are currently collecting x-ray data on another specimen and still anticipate ultimate success.

The remainder of this report is organized according to results rather than goals, but the relevant goals in the above list are indicated where appropriate.
Heating at various temperature in various atmospheres, deuteration, various wet chemistry procedures, i.r. analyses, and the Rietveld analysis (whole pattern fitting) method of x-ray and neutron powder diffraction patterns have been used both to study TE directly and to study it in comparison to hydroxyapatite, "OHAp". We first report results for particular components of TE.

\[ \text{CO}_3^{2-} \]

It was shown (paper #3, above) that, upon heating, \text{CO}_3^{2-} loss from TE begins at a much lower temperature (e.g., 100°C) than previously suspected. This fact probably has implications to site-separation for tooth restorations. An interconnectedness of A and B sites for \text{CO}_3 was demonstrated which may have significance in vivo. In the range 200-800°C, a substantial fraction of the B-\text{CO}_3^{2-} moves to A sites, apparently via a \text{CO}_2 intermediary, before being evolved. For the first time, a reasonably successful direct determination has been made of the locations of any \text{CO}_3 in TE or apatite. In paper 4, above, probable \(x, y,\) and \(z\) coordinates were deduced for A-\text{CO}_3^{2-}, that replacing 2\text{(OH)}^- in apatite. This was done from Rietveld analyses of powder diffraction patterns of carbonated-apatite specimens prepared at 1,000°C. The results of Rietveld analysis of TE heated to 800°C in N_2, in which enough A-\text{CO}_3^{2-} has been generated to expand the a axis by ~0.02 Å, are consistent with this A-\text{CO}_3^{2-} location. [Goals 2 & 3]

In A-type carbonate apatite, there is one \text{CO}_3 per unit cell and these \text{CO}_3 units take up ordered positions, as shown by the occurrence of the 00.1 reflection in, especially, neutron diffraction patterns (paper #4). The structure's space group is, then, no longer P6_3/m, but perhaps P6/b or even lower symmetry. With specimens from Dr. Bonel in Toulouse, Dr. Elliott has been working on this problem. In Sr carbonate apatite, the carbonated form shows two non-P6_3/m features, \(b=\pm a\) (nor 2a) and the occurrence of the 00.1 reflection. On heating through a
presumed phase transition at 200-300°C, these two feature disappear at different temperatures. Thus, the structure of carbonate apatite has some as-yet undetermined complexities. [Goal 2].

H₂O in TE

Further results have been obtained for both the role and the location of the few wt% H₂O that is structurally incorporated in TE. [Goal 2].

Pyrolysis experiments carried out with rather small temperature increments showed a "sudden" loss of ≈1/3 of the incorporated H₂O to coincide, within 25°C experimental error, with a "sudden" 0.014 Å contraction of the a lattice parameter. This finding adds weight to the hypothesis of LeGeros, Bonel, and Legros (Calcif. Tiss. Res. 26, 111-118 (1978)) that incorporated H₂O is responsible for a of TE being ≈0.02 Å larger than a of OHAp. However, it was found that a re-ordering was also involved in this contraction, so it is possible at this time only to say that the loss of H₂O and the a contraction are associated. It well may be later, but at this point a cause and effect relationship has not been established.

The structural location of the incorporated H₂O was suggested (paper #1) to be approximately midway between Ca(2) and O(3) triangles on the hexad axis, in some orientational disorder. Many Rietveld analyses (powder diffraction) of variously heated TE specimens tend to corroborate that suggestion, but the issue is really not yet settled (see abstract #4, above). One of the points needing resolution is that of what, precisely, is left behind when the H₂O leaves the structure. Both x-ray and neutron powder diffraction patterns are being used in that analysis. Dr. David Cox of Brookhaven National Laboratory has kindly provided some neutron diffraction patterns, of some of our specimens, to augment those we have collected here.
"Acid phosphate" is generally agreed to be an important entity in TE, but it is rather resistant to direct study. We have not yet been able to model it in TE in our Rietveld refinements with powder diffraction data. Its main i.r. band appears to superimpose on an ever-present CO$_3^{2-}$ band. In our pyrolysis studies reported in paper #3 we may have seen and followed its effect in i.r., but it is difficult to be sure. The effect followed was an apparent contribution to the 879 cm$^{-1}$ band attributable primarily to A-CO$_3^{2-}$. It seems improbable, though not impossible, that the superposition would be so exact. The pyrophosphate found HPO$_4$ thermal reaction was shown by x-ray diffraction to be β form, but the corresponding principal resolvable i.r. band was too weak to be discerned. Clearly, that elusive entity will have to be the object of much more study. [Goal 2].

**TE vs OHAp**

A substantial effort comparing TE and OHAp is in progress. Scores of Rietveld analyses have been carried out on variously prepared TE and OHAp specimens. Both OHAp and TE show some variability. In fact, the possibility is arising that we may be able to make useful differential studies of TE of different origins via the Rietveld-analysis method with powder diffraction patterns. However, the TE vs OHAp differences are generally greater than these internal variabilities, and informative comparisons have been made already (see abstract #2). One difference is in the location of the (OH)$^-$ along the z axis; it seems to be near $z = 0.13$ in TE instead of 0.19 as in OHAp. Another difference is that the $\approx 0.02$ Å enlargement (removable by heating) of the a lattice parameter in TE and in OHAp prepared by a reflux method can not be due to the same mechanism. It is hoped that further detailed Rietveld-analysis comparisons of TE and OHAp will lead to good trial models for the structural locations of HPO$_4$ and B-CO$_3^{2-}$ [Goal 4 & 2].
Structural OH⁻

Documentation of the deficiency of structural OH⁻ in TE continues to increase. From re-hydroxylation experiments reported in paper #4, the initial deficiency was estimated to be >20%. The increase of structural OH⁻ with increasing pyrolysis temperature, reported in paper #3, indicated ~40% initial deficiency. This is a very intriguing subject, because the mechanism(s) of this deficiency are not yet known.

OHAp variability

Preparations normally labelled "hydroxyapatite" have been shown to differ markedly according to the preparation method and procedural details. Rietveld analysis results, i.r. features, heating effects, deuterizability, solubility, differences in Ca/P ratio and differences in phase are being inter-correlated. These will be described in a paper soon to be prepared. Some of these correlations are touched upon in paper #6. One very interesting thing that is emerging is some beginning insight into the diffusion process along the X-ion channels. When the OH⁻ ions are all present and ordered, diffusion is very slow. When OH⁻ ions are missing and the remaining ones show some disorder, then, unless "pinning" ions (e.g., F) are present, diffusion takes place very readily. We expect a full understanding of the inhibition and enhancement of diffusion, in the X-ion channels, to have significant implications to in vivo situations, e.g., cariogenicity and cariostasis.

Sr in Ca Apatite

Because Sr is cariostatic, we have studied the structural effects of small amounts of Sr substituting for Ca in (Ca,Sr)ClAp. A single crystal study was
reported briefly last year. Two effects are of particular interest. One is the preferential substitution of Sr at the Ca(2) site, rather than Ca(1), when small amounts of Sr are present. Thus, we can expect that the little Sr present in TE is at a Ca(2) site, bordering the X-ion channel. The second effect is that which Sr$^{2+}$ exerts on the Cl$^-$ ion location. On average, the Cl$^-$ ion location is shifted steadily from $z = 0.44$ to $z = 1/2$ with increasing Sr, but (a) the initial amounts of Sr have the greatest effect and (b) the shift of a Cl$^-$ ion adjacent to a Sr$^{2+}$ ion is undoubtedly much greater than the average. Thus, the effect of Sr$^{2+}$ on adjacent X-ions may be the principal way in which a very minor amount of Sr expects its cariostatic effect.

The single crystal work on (Ca,Sr)ClAp has now been written up and accepted (paper #2), but these possible implications to cariostatic actions were not stated in that paper.

**Methodology development**

Much of what we aspire to do seems to be at or slightly beyond the state-of-the-art of some particularly promising technique in which we have expertise. Hence, we develop and extend methodologies. Our greatest such effort in recent years has been with the Rietveld method of whole-pattern-fitting structure-refinements from powder diffraction data. [Goal 1].

The computer program reported on last year has now been completed through the multi-phase (2 phase) capability (version DBW 2.8). Referred to as the DBW program, it is in constant use, and has now produced several hundred Rietveld refinements. It has been distributed to other users. At the same time, further improvements are being made in it. It is a necessarily large program (>5,000 FORTRAN statements). It represents a major accomplishment for its author (D.B. Wiles) and a major asset.
to the project. Mr. Wiles gave a paper (oral) on it at the March 1979 Am. Cryst. Assoc. meeting, where it generated a lot of interest.

With the convenience of the DBW program, it has been possible for a great many Rietveld analysis to be made of TE and related apatite specimens. This has provided a data base which allows one to assess the strength and limitations of the Rietveld method and to see where improvements can be made. This is an on-going process. As understanding develops, other workers are interested in our findings, so we get invited to give talks about them in which the project is credited (e.g., paper #5, seminars in Toulouse and Milano last July, other invited talks coming up).

Collaboration and cooperation abroad

Dr. J.C. Elliott of London spends a few weeks with us each summer. Each visit is very productive and collaborative work continue when he returns to London. Last summer, just at the point of completing the space group assignment and powder-pattern indexing for A-type carbonate apatite, he turned up the unexpected complexity of the material. He continues to work on this problem in London. He also consults, discusses and collaborates with us.

Collaboration with Dr. Montel and Dr. Bonel of Toulouse continues to be fruitful. During the PI's visit there last July, Dr. Bonel and he were able to work through several matters and to reach agreements on the final form of the paper, now accepted, listed as paper #4.

A July visit by the PI to Karlsruhe, Germany, to Professor Wondratschek and his colleagues also made possible very fruitful discussions. The principal focus of these discussions was the discrepancy between Dr. Engel's chemical results...
and our published x-ray-structure-refinement results for the halogen deficiency in several Cd apatite crystals which Dr. Engel had provided for our study some years ago. This problem had been bubbling for several years, some hostility had developed, and correspondence had not been an adequate means to get at the difficulties. Dr. Engel came over for the day from his present employment about 150 km away. The reasons for the discrepancy were not identified but some possibilities were suggested, mutual trust and sense of collegiality were restored, and investigative steps to be taken by each group were listed. Particularly useful to us was Professor Wondratschek's suggestion that a halophosphate might be forming. That could explain the discrepancy. More importantly, the halophosphate suggestion has implications to many of our other apatite and tooth enamel studies. It is clearly a possible structural entity that should be very carefully assessed, especially in non-stoichiometric apatites (the usual kind). Thus, this conference (~6 hrs) was extraordinarily fruitful for our apatite and tooth enamel project.

3. Significance

Development of understanding of mechanisms of dental health and disease at an atomistic level will provide a necessary base for interrupting or adjusting these mechanisms to modify, in this case, the behavior of tooth enamel both toward disease and dysfunction vectors and toward accommodation of restorative materials.
4. Research goals for the coming year

The work during the coming year will be logical continuation and extensions of present thrusts. Some of the things that will receive emphasis will be to:

1) do Rietveld analyses of TE with improved models both for TE and for the profile functions
2) make more detailed comparisons of TE and OHAp
3) prepare a paper on OHAp variability
4) bring to the write-up stage the work on F and Cl effects on OH diffusion in synthetic OHAp
5) continue to improve the certainty and range of applicability of the Rietveld method
6) make further studies to pin down the location of the structurally incorporated H_2O in TE and its roles with various phenomena
7) complete single crystal structure analysis of CaCl_2-deficient ClAp, try to convert it to Ca(OH)_2 deficient OHAp and analyze that
8) continue giving attention to ongoing concerns such as
   a) mechanism of OH deficiency
   b) mechanisms of X-ion diffusion
   c) possible role of halophosphates
   d) structural aspect of B-CO_3

The undersigned agrees to accept responsibility for the scientific and technical conduct of the project and for provision of required progress reports if a grant is awarded as the result of this application.

13 February 1980
Date

R.A. Young
Principal Investigator or Program Director
Publications: (continued)


P13 "Variability of Hydroxyapatite Preparations", R.A. Young and D.W. Holcomb, (submitted)

(c) Other

Four major project-based invited papers were presented orally at scientific meetings and led to papers P10 (1980 Denver Conference on X-ray Analysis), P13 (1981 Gordon Conference on Calcium Phosphates), P11 (XIIth International Congress of Crystallography, August 1981 in Ottawa), and P12 (Dahlem Konferenz on Biological Mineralization, October 1981 in Berlin). Two lesser invited papers were presented at other meetings. Four different colloquia on project work were presented at four different institutions in Japan in June 1980 (at no cost to the project).

2. Two reprints, each, of publications P1 through P13 are enclosed with the original of this application.

3. Progress Report

(1) The general scientific goals of the project are unchanged.

(2) Studies and Results

Synthetic hydroxyapatite, "OHAp," is widely used as a starting, chemical reference, and model material in the biological apatite field. It is, therefore, important that the material synthesized be well characterized and reproducible from synthesizer to synthesizer. Unfortunately, it is not easy to prepare hydroxyapatite that is sufficiently near to stoichiometric for it to be really suitable for these uses. Worse, this fact is widely unappreciated outside of a rather small group of apatite chemists.

In fact, the differences among preparations reported to be hydroxyapatite might lead one to wonder whether there really is such a thing as pure, stoichiometric hydroxyapatite, Ca$_5$(PO$_4$)$_3$OH.

We have therefore, made a point of assessing just how hydroxyapatite prepared in various oft-used ways exhibits marked differences with preparation method. Specimens were prepared with two precipitation methods, a reflux method, a hydrothermal method, a high temperature (1000°C) solid-state reaction method, and by conversion of chlorapatite at 1000°C. They were compared in detail by use of several techniques, the major ones being x-ray diffraction including Rietveld structure refinements, quantitative i.r. analyses, and deuteration kinetics studies. At least some of the specimens differed with respect to each of the 14 properties measured. The principal properties assessed were (1) lattice parameters, (2) Ca/P
ratio, (3) OH\textsuperscript{-}-site filling, (4) OH\textsuperscript{-} disorder, (5) content of (a) structurally incorporated H\textsubscript{2}O, (b) HPO\textsubscript{4}\textsuperscript{2-}, (c) CO\textsubscript{3}\textsuperscript{2-} and (d) other substitutions or second phases, (6) crystalline phase (i.e., monoclinic or hexagonal), and (7) ease of diffusion along the "X-ion channels," the "channels" in which the structural OH ions of OHAp are centrally located. The major lattice parameter differences could be largely accounted for by structurally incorporated H\textsubscript{2}O, CO\textsubscript{3}\textsuperscript{2-}, and O\textsuperscript{2-} for 2(OH).

Deuterizability was used as an indicator of ease of diffusion along the X-ion channels, a property that may be related to dissolution kinetics. The differently prepared specimens differed in deuterizability by at least two orders of magnitude. The high temperature preparations, which were monoclinic, deuterated very little at 110°C, even in 1000 hours. The precipitated and reflux specimens deuterated readily. There were general indications of correlation between ease of diffusion and features providing passing sites for the species diffusing along the X-ion channels, e.g., OH\textsuperscript{-} disorder, vacancies and distortions in the walls of the X-ion channels (mostly by CO\textsubscript{3} for PO\textsubscript{4}), and, possibly, OH\textsuperscript{-} vacancies.

Correlation of structural H\textsubscript{2}O, present in the aqueous preparations, with ease of diffusion is still ambiguous. It seems possible that the H\textsubscript{2}O structurally incorporated in human tooth enamel (TE) may be present in two sites, only one of which affects the a-axis dimension. (The TE unit cell has an a lattice parameter ~0.02Å greater than that in OHAp. It is also notable than TE deuterizes much more readily than does OHAp prepared by the hydrothermal or high temperature methods.) Much of the results obtained to date on this subject are reported in paper P14, a relatively major paper.

Building on the base described above, it is now possible to focus studies on the effects, on diffusion, of specific atomic substitutions and disorder features. The effects of F\textsuperscript{-} and Cl\textsuperscript{-} on diffusion along the X-ion channels are now being studied explicitly. Further studies are being planned to elucidate, in terms of atomic-scale mechanisms, the effect of CO\textsubscript{3} substitution both in the X-ion channel ("A-site") and in the channel walls ("B-site", CO\textsubscript{3} for PO\textsubscript{4}). Also being pursued are the structural location(s) of H\textsubscript{2}O in human tooth enamel (TE) and its role, if any, in diffusion of various species along the X-ion channel.

In areas other than hydroxyapatite variability and the diffusion mechanism in apatites and TE, our principal achievements in this reporting period relate to advances in (a) atomic detail determinable and (b) correct assessment of the reliability of such determinations from the powder diffraction patterns (x-ray and neutron) with which we must work, since single crystals of TE are not available. Improvements in our use of the Rietveld whole-pattern-fitting structure-refinement method have been realized through (a) identification and use of improved profile shape functions (P11), (b) implementation of simultaneous refinement of background parameters, and (c) incorporation of a refineable preferred orientation parameter in our computer program. Work on profile functions is being continued with a view toward still better functions (and their implementation) which will permit determination of additional information detail and, in particular, crystallite size and strain parameters as an incidental product of Rietveld structure refinement. If this can be accomplished satisfactorily, it should be of real benefit in the characterization of tooth and bone specimens of different origins, life history, and biological properties.
The distinction of false from real differences is an ever-present problem in any scientific study. In our case, there has been a particular problem with knowing how reliable are the atomic scale details obtained in our structure refinements, e.g., atomic coordinates (positions), site occupancies, and thermal vibration parameters. Estimated standard deviations are calculated, according to standard statistical methods, as a part of our Rietveld structure refinement process. The Rietveld method is still new, still under development, however. Recently the validity of these calculated estimated standard deviations (c.e.s.d.'s) has been called into question. M.J. Cooper in particular (e.g., Sakata and Cooper 1979) claims that it is inherent in the Rietveld method that the c.e.s.d.'s are always calculated too small. Other workers (e.g., Prince, 1981; Hewat & Sabine, 1981) deny this. Because of the importance of this point to our permitted interpretations of our Rietveld structure refinement results (which, in turn, are of major importance to the project), we have undertaken our own tests of this point.

Direct statistical test of correctness, as calculated with our program DBW 3.2, has been made by refinement with calculated "data" to which random errors have been added. From structural models refined from experimental data, calculated step-scanned x-ray powder diffraction patterns were generated with the pseudo-Voigt profile function and non-structural parameters set at the values obtained in the refinement. By adding different random errors, 20 different sets of "data" were then generated for quartz and for dickite, each, and 40 each for 5 different sets of experimental conditions for fluorapatite. With these data, Rietveld refinements (240) were carried out for the 5 to 43 structural and -17 non-structural parameters. For each set of 20 (or 40) values for each parameter and condition set, a "measured e.s.d." (m.e.s.d.) = \( \frac{1}{n-1} \sqrt{ \sum (x - \bar{x})^2 } \) was determined. For the structural parameters, the ratio m/c of m.e.s.d. to c.e.s.d. was found to be 1.5(5) at the 95% confidence level for dickite and fluorapatite and nearer 2.0(7) for the 5 quartz structural parameters. The ratio was near 0.9(3) for background parameters and 1.0(3) for lattice parameters. If overlap were the cause of m/c being > 1, one would have expected quartz to show the smaller m/c.

Because of these tests, carried out on our own particular materials of interest with our own computer program, we now have a solid basis for distinguishing significant from non-significant differences in the results we obtain about atomic-scale details in TE and apatite.

With these improvements in both precision obtainable and in our assessment of its reliability, we are now returning to the question of changes in crystallographic details in TE as a function of temperature and of humidity. The hope is that so-induced atomic-parameter changes can be discerned and followed and will thus lead us to a better understanding of the roles of HPO₄ and H₂O, in particular, in TE. A first step in this renewed effort is redoing, in the improved manner, the Rietveld refinements of TE with some 30 sets of x-ray powder diffraction data previously (three years ago) collected over the range 25°C-500°C under vacuum. Later, different combinations of atmosphere with temperature will be tried.

Particularly with the help of the new data handling and display unit now on order for our i.r. unit, we also look forward to improved determination of atomic-scale details and ionic interactions via infrared spectroscopic studies.
SECTION IV—SUMMARY PROGRESS REPORT

APPLICANT REPEAT GRANT NUMBER SHOWN ON PAGE 1

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Last, First, Initial)

R. A. Young

NAME OF ORGANIZATION

Georgia Institute of Technology

PERIOD COVERED BY THIS REPORT


TITLE (Repeat title shown in Item 1 on first page)

Tooth Enamel Apatite at the Atomic Level

1. List all publications, not previously reported, resulting from work supported by this grant (author(s), title, page numbers, year, journal or book). List manuscripts separately as submitted for publication or accepted for publication.

2. Provide two reprints of publications not previously submitted to the awarding unit.

3. Progress Report. (See instructions)

1. Publications

(a) Full papers previously reported as "in press" or "submitted" and now published.


(b) Full papers not previously reported:


2. Reprints

Two reprints, each, of publications P1-P5 are enclosed with the original of this application.
3. Progress Report

(1) The general scientific goals of the project are unchanged.

(2) Studies and Results

The diffusion of various atomic species along the "channels" in apatite and tooth enamel (TE) is, apparently, a very important process in the physico-chemical functioning of those materials. The ease of diffusion, as measured by deuterizability, varies by orders of magnitude among the differently prepared specimens of "hydroxyapatite" (P3). Within this spectrum of variability, diffusion in TE takes place with relative ease. TE contains amounts in the range 2-5 wt% each of CO3, HPO4, and H2O and usually a few tenths wt% of F and Cl. Our work has suggested that at least some of these things may have significant effects on the ease of diffusion through the channels in TE by a mechanism of providing sites in the walls where diffusing species may bypass one another.

Compared to hydroxyapatite (OHAp), TE has an a axis expanded by about 0.02 Å. The questions are (1) what is responsible for this expansion and, particularly, (2) what might be in the channels that is both causing the expansion and contributing to the easy diffusion of ionic species along the channels? On the basis of apparent correlation of loss of substantial amounts of the "structural" H2O with lattice contraction on heating, it had been suggested (LeGeros, Bonel, and Legros, 1978; Holcomb and Young, 1980) that the structurally incorporated H2O was responsible for most of the lattice expansion (followed by contraction on heating). It had even been suggested (Young and Mackie, 1980) that the responsible H2O might be structurally incorporated in the channels. However, that has not been proven. The major candidates, because of the relatively large amounts of them present, for responsibility for the lattice expansion are HPO4, CO3, and H2O. Neither A site nor B site CO3 changes dramatically in the narrow temperature region in which the lattice parameters of TE do (Holcomb and Young, 1980). In that work on TE, HPO4 content could not be followed conveniently because the i.r. band overlapped with the CO3 band. In more recent work (Young and Holcomb, 1982) it was found that hydroxyapatite prepared by hydrolysis of CaHPO4 contained structural water and HPO4, but no CO3. We have, therefore, studied this convenient system to determine the effect of HPO4, on lattice parameters and, particularly, the effect which loss of HPO4 has on lattice parameters in the same temperature regime in which the lattice contraction was found in TE (approximately 250-300°C). This study has resulted in paper P5, in which it is reported that most of the HPO4 is lost between 160°C and 240°C and is accompanied by an a lattice-parameter contraction of 0.0043 Å.

Contrary to the situation in TE, no major "precipitous" loss of structural H2O was documented, though a small one may occur in the range 240-300°C. Loss of H2O began at about 240°C and continued past 500°C. Thus, in this system, the separate effects of HPO4 and H2O on lattice parameters were distinguished. It has been concluded that loss of HPO4 cannot be a major contributor to the approximately 0.014 Å lattice contraction found in TE between 250 and 300°C (Holcomb and Young, 1980).
This still leaves structural H$_2$O as the prime suspect for the expansion of the lattice of TE (or, rather, that part which is removed by heating the TE to 300°C). But just how it may do so is still not known because the structural location(s) of the structurally incorporated H$_2$O molecules has (have) not yet been definitely determined. Although the precision in our determination of structural detail in these materials has been improved considerably in the last few years, still more precision is needed to answer these questions.

Also present in TE are small amounts, a few tenths wt%, of F and Cl. These, too, have an effect on diffusion of ionic species along the channels. We are in the process of doing long-term studies, via deuterizability, of the effect of both of these ions on diffusion along the channels. Both have a retarding effect. The process of the diffusion exchange is being followed with infrared band intensities. One complication is that the presence of both F and Cl seem to change the oscillator strength, somewhat, of the OH stretch oscillations which give rise to the principal band followed (3570 cm$^{-1}$). Thus, simultaneously, we are having to quantify the effect of the F and of the Cl, both separately and jointly, on the OH oscillator strength.

Since our Rietveld refinement technique had been improved with improved profile functions, we thought it might be worthwhile to redo the structure refinements with the 30-odd sets of data taken a few years ago on tooth enamel as a function of temperature. The hope was to find some changes in atomic detail accompanying the changes in lattice parameter in the 250-300°C range. While our precision was better this time than before, it is still not sufficient to determine the atomic scale details accompanying the lattice contraction. More work is needed, both with improving the precision in the technique and, probably, in collecting data on new samples.

One way to improve the precision and structural detail obtainable from the powder diffraction data is to make use of the pulsed neutron technique. Unlike fixed energy methods, this method allows collection of data with good resolution over an extended range in sin θ/λ. There have been reports of precision in atom positions, determined with this technique, which are essentially equal to those from good single crystal refinements (Jorgenson, 1982). Therefore, we prepared a proposal to use the Intense Pulsed Neutron Source (IPNS) at Argonne National Laboratories. Our proposal was accepted and in April of this year Mr. Paul Suitch spent two weeks at the IPNS collecting data and undertaking the analyses. Unfortunately, the analyses had to be done on the local VAX computer; the programs and accompanying support files were not portable. This lack of portability has precluded us from finishing the refinements up to the current time. Preliminary results are, however, promising. We are very hopeful that we may be able to locate the H of the HPO$_4$ in TE from refinements with these data taken both on deuterated and undeuterated TE at both room temperature and 10°K. Just at the end of this reporting period, the IPNS people had prepared their program and files in such a manner that it could, possibly, be used at other installations. We now have a copy and will try to use it on the VAX computer here on our campus.
Because the specimens of greatest interest, particularly TE, cannot be available as single crystals, the Rietveld whole-pattern-fitting structure-refinement method for determining structural details from powder diffraction patterns has been and continues to be crucial to our progress. The need for improved precision in the structural details determined is indicated above. Thus, we continually are working on the method itself (which is still rather new) and its methods of application in order to improve the precision. At the same time, however, it is necessary that one know very well just how good (or bad!) is the precision which is being obtained in the structure refinements. Thus, for example, it is very important for us to know whether the standard deviations calculated by the program are actually correct, and therefore truly indicate the minimum probable error which we can count on in comparing results from different data sets. As was mentioned in the last annual report, there have been several allegations in the literature that these calculations were not correct. We have, therefore, undertaken an extensive series of direct statistical tests of correctness, as we said in the last annual report we had started to do. Much more work has now been done, a bug in our computer program has been found and corrected, and the result is that we have been able to show that the standard deviations, are, in fact, calculated correctly in this Rietveld approach. These results have been offered for publication as paper P4. This new finding represents a correction to the preliminary findings stated on page 8 of the last annual report in which it was stated that there seemed to be a factor of 1.5 between the actual and calculated standard deviations. That factor was traced to the program bug mentioned above. The standard deviations calculated in the Rietveld method do, in fact, represent accurately what they are intended to represent. They do not, of course, represent any errors arising from other than random errors.

There remain some unexplained peculiar sensitivities of some parameters to others when we are applying the Rietveld method of structure refinement. We have previously noted and commented on the fact that a rather small preferred-orientation correction had an effect on the apparent scattering density along the channels far beyond any indicated by the correlation matrix. A similar sensitivity not reflected in the correlation matrix has now been found between the 2θ-zero correction parameter and the absolute values of the lattice parameters obtained. (The ratio a/c of lattice parameters is far less affected.) Part of our program for the ensuing year will be to try to find and remove the causes of these sensitivities which are not reflected in the correlation matrix and, therefore, not in the standard deviations.

Because of the potentially considerable importance of octacalcium phosphate (OCP) in tooth and bone, we have been interested in the possible application of the Rietveld structure refinement method to it both to corroborate the single crystal results of Brown and, potentially, to make it easier to pinpoint significant small structural differences among preparations of OCP both in conjunction with and separately from apatites. Unfortunately, it is a very complicated structure for the Rietveld method to handle conveniently. Because there are so many atoms in the asymmetric unit, the ratio of parameters-to-be-refined to information-
available is not particularly favorable. However, we have at least progressed to the point that we have been able to refine the non-structural parameters, the lattice parameters, the background parameters, and the calcium atom parameters well enough so that we have a calculated diffraction pattern that fairly well fits our observed x-ray powder diffraction pattern for OCP kindly supplied by Dr. W. E. Brown. The structural (i.e., atomic positional) parameters which permitted this degree of good fit ($R_{wp} = 28.7\%$, $R_B = 7.4\%$) were those provided by Dr. Brown with the exception that we were able to refine the positional parameters for the eight calcium atoms (no real improvement). While this problem of doing structure refinements on OCP is interesting, we tend to keep it in a background mode because of the large computational costs associated with it.

There are still many outstanding questions about the role of carbonate in tooth enamel which we hope to be able to address with some expectation of success. Two of the simplest are the exact locations of CO$_3$ in the channels (A sites) and of CO$_3$ substituting (everyone presumes) for PO$_4$ (B sites). As the Toulouse group has shown, there is a lot of interaction between (1) the kinds and amounts of substitutions and their effects on lattice parameters and (2) the presence or absence of sodium and flourine. In discussions with the Toulouse group, it has become clear that we can make better progress on these questions with a joint effort, pooling our particular expertises. To this end, the PI expects to spend some time in Toulouse in the coming year working on these and related problems with the Toulouse group.