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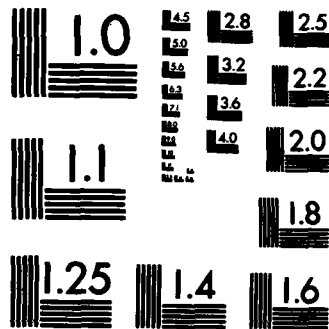
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**MANAGEMENT OF HARD TISSUE AVULSIVE WOUNDS  
AND MANAGEMENT OF OROFACIAL FRACTURES****ANNUAL REPORT****Larry G. McCoy and Craig R. Hassler****July 15, 1977****Supported by****U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND  
Fort Detrick, Frederick, Maryland 21701-5012****Contract No. DADA17-69-C-9118****BATTELLE  
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) <i>in bioceramics</i> Research studies were continued to further our understanding of the <u>in vivo</u> behavior of resorbable calcium phosphate ceramics for use in the management of hard tissue avulsive wounds and orofacial fractures.			

Material processing studies were conducted to develop porous tricalcium phosphate materials of different stoichiometry. These two portions of the study were to further understanding of the basic question: Is the optimal material for bone ingrowth and biodegradation going to be produced by alterations in stoichiometry or alterations in pore structure within the material of the given stoichiometry?

Numerous tricalcium phosphate powders were produced having controlled calcium to phosphate ratios. Specifically, three powders were prepared using the standard technique of modifying composition of tribasic calcium phosphate powders by the addition of phosphoric acid. After three powders of various composition were made at Battelle, the powders were mill-blended and submitted for verification analysis. Materials were then fired and analyzed by X-ray defraction to determine the crystalline phases that might be present in the finished implants. The results of the study indicated that preparation of a single phase variable composition material does not appear possible using standard methods even though beta phase tricalcium phosphate will be the predominant phase in all materials, secondary phases of monetite or hydroxyapatite were always found depending upon what border of the compositional range the compound fell. Consequently, these three different materials were not developed further. It was recommended that pore structure conformation be studied.

ABSTRACT

This report summarizes results of continued studies for further developing and understanding the in vivo behavior of resorbable calcium phosphate for use in the management of hard tissue avulsive wounds and orofacial fractures.

Specific studies have been devoted to the preparation and evaluation of tricalcium phosphates having various altered stoichiometries.

This study concluded that a single phase variable composition material could not be produced. Therefore, it was suggested that resorption rate alteration be attempted by varying the pore distribution and configuration of the material.

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## SUMMARY

Research studies were continued to further our understanding of the in vivo behavior of resorbable calcium phosphate ceramics for use in the management of hard tissue avulsive wounds and orofacial fractures.

Material processing studies were conducted to develop porous tricalcium phosphate materials of different stoichiometry. These two portions of the study were to further understanding of the basic question: Is the optimal material for bone ingrowth and biodegradation going to be produced by alterations in stoichiometry or alterations in pore structure within the material of the given stoichiometry?

Numerous tricalcium phosphate powders were produced having controlled calcium to phosphate ratios. Specifically, three powders were prepared using the standard technique of modifying composition of tribasic calcium phosphate powders by the addition of phosphoric acid. After three powders of various composition were made at Battelle, the powders were mill-blended and submitted for verification analysis. Materials were then fired and analyzed by X-ray defraction to determine the crystalline phases that might be present in the finished implants. The results of the study indicated that preparation of a single phase variable composition material does not appear possible using standard methods even though beta phase tricalcium phosphate will be the predominant phase in all materials, secondary phases of monetite or hydroxyapatite were always found depending upon what border of the compositional range the compound fell. Consequently, these three different materials were not developed further. It was recommended that pore structure conformation be studied.



## FOREWORD

This study has been conducted at Battelle's Columbus Laboratories utilizing the talents and resources of the Ceramic Materials Section and the Bioengineering/Health Sciences Section. This is an Annual Progress Report under Contract No. DADA17-69-C-9118, "Management of Hard Tissue Avulsive Wounds and Management of Orofacial Fractures". The Principal Investigator for this research was Mr. Larry G. McCoy.

We would like to acknowledge the valuable assistance of Mr. Roger K. Beal for his excellent work in preparation of the porous implant materials. Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

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## BACKGROUND, PROBLEM AND APPROACH

Historically, various techniques have been employed for the repair or treatment of osseous diseases, defects, and wounds. Autogeneous bone grafting remains the most satisfactory approach but is not without the disadvantages associated with double surgeries and the limitations imposed on the repair of massive osseous defects.

Since April, 1970, Battelle's Columbus Laboratories has been conducting research under contract with the Dental Research Division, U.S. Army Medical Research and Development Command, on the development of resorbable ceramics for potential application in the repair of hard tissue avulsive wounds. The basic materials have been calcium phosphates. These materials were selected because they contain two of the essential elements of the natural bone mineral phase, calcium hydroxyapatite.

In vivo studies were conducted initially at U.S. Army Institute of Dental Research (USAIDR), using the sintered porous materials and slurries prepared at Battelle from tricalcium phosphate  $\text{Ca}_3(\text{PO}_4)_2$  and other calcium orthophosphate powders  $\text{CaHPO}_4$  and  $\text{Ca}(\text{H}_2\text{PO}_4)_2$ , to evaluate the potential use of calcium phosphates to both facilitate repair of bone defects and to determine the best material for future exploration<sup>(1-3)</sup>. The implant studies indicated that calcium phosphates consisting essentially of the mineral phases  $\text{Ca}(\text{PO}_3)_2$ ,  $\text{Ca}_3(\text{PO}_4)_2$ , and  $\text{CaHPO}_4$  are well tolerated by the tissue, appear to be nontoxic, are resorbable, and permit rapid invasion of new bone.

Of the various porous calcium phosphate materials investigated, tricalcium phosphate,  $\text{Ca}_3(\text{PO}_4)_2$ , was selected for continued development and evaluation since it was easy to fabricate and was found to be both biocompatible and resorbable. Emphasis has been directed toward producing low-density porous materials consisting of single-phase tricalcium phosphate<sup>(4-7)</sup>.

Although previous implant studies at USAIDR have demonstrated that porous tricalcium phosphate is biocompatible, resorbable, and promotes or permits rapid ingrowth of new bone, histological evidence indicated persistence of a residual ceramic structure as long as 1 year after implantation. This structure appeared to be composed of an isomorphous distribution of small encapsulated ceramic particles. The presence of this residue would be

expected to retard complete remodeling of the bone and the attendant strength development.

As a result of this problem, the primary emphasis of continued studies was directed toward the development of porous materials having improved (increased) resorption rates. This objective may be achieved either by changes in structure or chemistry of the ceramic implant material.

To provide basic resorption rate data on the in vivo behavior of the tricalcium phosphate bioresorbable ceramics, implant studies were initiated in 1975 at BCL using the rabbit calvarium model(8). Historic samples of tricalcium phosphate were implanted as a control and samples of two new materials were implanted for comparative observation. These new materials were prepared using the improved processing techniques derived in previous materials development studies and represented significant improvements in the structural characteristics of porous tricalcium phosphate. The characterization of the materials involved and the results of the in vivo studies were the subject of the Fifth Annual Report(8).

These results indicated that the improved material exhibited significant increases in resorption rate. In fact, the material resorbed so rapidly that after the ninth month the implant appeared to be granulated and was invaded with connective tissue. This result does not imply lack of biocompatibility but does suggest that such rapid degradation can be deleterious in stress-bearing situations. It is not known whether the enhanced resorptivity resulted from achieving a Ca/P ratio closer to the theoretical for tricalcium phosphate or from the improvements in the structural characteristics of the material.

The objective of this years effort was to prepare materials with minor variations in chemical composition so that the resorption rate of porous tricalcium phosphate materials which have identical pore structures could be ascertained. For this study, it was necessary to prepare new tricalcium phosphate powders having controlled Ca/P ratios. However, to achieve a structurally sound and single phase ceramic, the composition of the new powders must lie within a very narrow  $\beta$ -C<sub>3</sub>P (beta tricalcium phosphate) solid solution region.

## MATERIALS, METHODS AND RESULTS

### Variable Stoichiometry Materials Development

To discern the effect of chemistry, it was sought to develop a tricalcium phosphate having variable stoichiometry. This was based on the observation of the  $P_2O_5$ -CaO phase diagram as proposed by Welch and Gutt, which showed a solid solution region at 800°C with a Ca/P ratio of 1.788 to 1.941 for tricalcium phosphate.

For this study, it was necessary to prepare new tricalcium phosphate powders having controlled Ca/P ratios. To achieve a structurally sound and single phase ceramic, the composition of the new powders must lie within the  $\beta$ -C<sub>3</sub>P (beta tricalcium phosphate) solid solution region shown in Figure 1. The composition range of the solid solution is quite narrow; the phosphorous content ranges from 20.0 to 20.8 weight percent (45.8 percent as  $P_2O_5$ ).

Three powders having the compositions designated A, B, and C in Figure 2 were prepared by the standard technique of modifying the composition of tribasic calcium phosphate,  $Ca_{10}(OH)_2(PO_4)_6$  by the addition of phosphoric acid. The nature of this method has necessitated reliance on an iterative formulation/analysis/adjustment procedure for producing precise compositions. For an analysis standard, a stoichiometric tricalcium phosphate composition was prepared using a chelometric standard grade of calcium carbonate (100.0 percent  $\pm$  0.05  $CaCO_3$ )\* dissolved in the appropriate concentration of a certified phosphoric acid (85 percent  $\pm$  0.05  $H_3PO_4$ ).

The end member powder compositions A and C were prepared first and were chemically analyzed for total Ca and P contents. Although the absolute values reported for both the Ca and P contents were below the targeted values, when the data were normalized on the basis of the known Ca/P ratios of the analytical standard, the results agreed quite closely with the targeted Ca/P ratio. Powders A and C were then mill blended in equal proportions to prepare

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\*Fisher Scientific, Inc., Pittsburgh, Pennsylvania.

CaO-P<sub>2</sub>O<sub>5</sub>

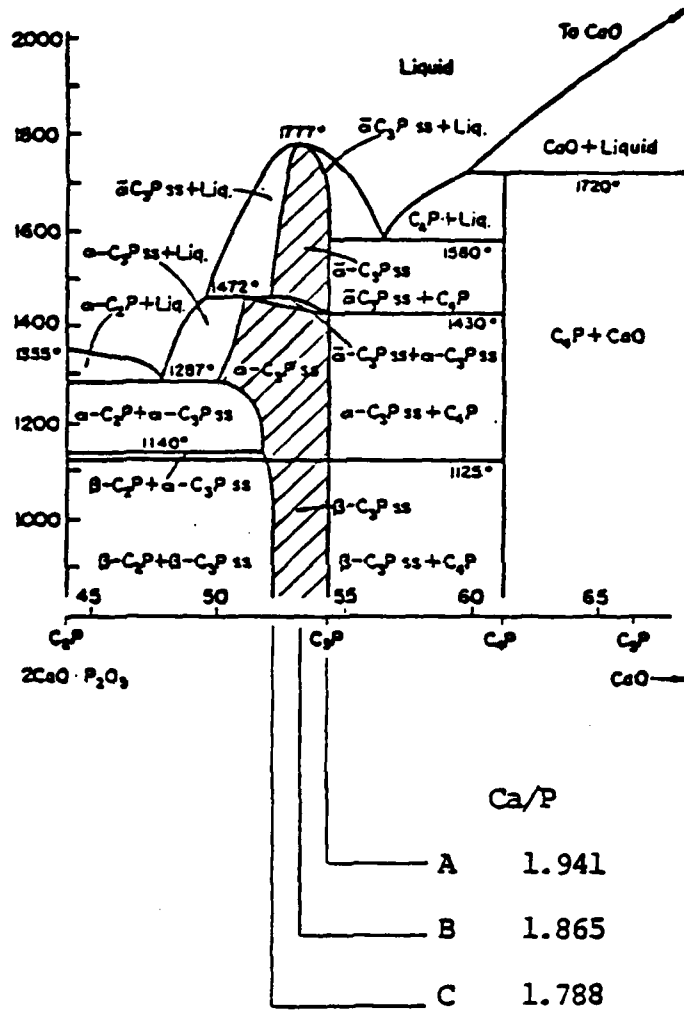


FIGURE 1. SYSTEM CaO-2CaO·P<sub>2</sub>O<sub>5</sub> C = CaO, P = P<sub>2</sub>O<sub>5</sub>

the intermediate B composition and samples of all three were submitted for verification analysis. The results of this second analysis were not consistent with the first. As a further check, a third set of samples was analyzed. After normalization on the basis of the known Ca/P ratio of the standard, the results somewhat verified the second analysis (i.e., all compositions were approximately 1 percent calcium rich). However, there was sufficient variation between the results (i.e., approximately 25 percent of the solid solution range) that significant doubt was generated as to the validity of the analysis procedures and/or the ability to produce sufficiently homogeneous powders by the standard procedure.

Although the validity of the above results was uncertain, standard procedures were continued toward the fabrication of porous implant specimens. After the firing, samples of each material were analyzed by x-ray diffraction to determine the crystalline phases that might be present in the finished implant.

Although  $\beta$ - $\text{Ca}_3(\text{PO}_4)$  was the predominant phase in all the materials, there were secondary phases of either monetite ( $\text{CaHPO}_4$ ) or hydroxyapatite  $\text{Ca}_{10}(\text{OH})_2(\text{PO}_4)_6$ , depending on what border of the composition range the composition fell. These results suggest that it is not possible to produce a nonstoichiometric tricalcium phosphate with typical low temperature sintering processes. It may be possible to quench melts of CaO and  $\text{P}_2\text{O}_5$  of the appropriate Ca/P ratio to achieve tricalcium phosphate of variable stoichiometry as is normally the procedure for determining phase diagrams. However, this is not a practical procedure for producing sinterable powders.

Since the preparation of single phase variable composition material does not appear possible, continuation of the chemistry versus resorption characteristics study is obviated. Although it is feasible to conduct implant studies with the present two-phase materials, the presence of these second phases would only confuse the interpretation of whether any observed effects were due to the tricalcium phosphate or the secondary phases. Consequently, further preparation of these materials was terminated and no implant studies were initiated.

CONCLUSIONS

From this study it appears that preparation of single phase variable composition is not possible. Even though two phase materials could be produced they would not serve the purpose of the study, to observe the effect of composition upon resorption rate in vivo. Consequently, these studies were terminated. It is recognized that the effect of pore size now be explored as a method of altering resorption rate.



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