JOURNAL OF MATERIALS SCIENCE: MATERIALS IN MEDICINE 1 (1990) 114–117

Post-composition control of hydroxyapatite in an aqueous medium

T. HONDA, M. TAKAGI, N. UCHIDA, K. SAITO, K. UEMATSU
Department of Chemistry, Faculty of Engineering, Nagaoka University of Technology, Kamitomioka 1603-1, Nagaoka, Niigata, 940-21 Japan

Composition control of hydroxyapatite by post-treatment in an alkaline solution was examined. Non-stoichiometric material having a Ca/P ratio of 1.60 was treated in distilled water (pH 6.5) and in a concentrated aqueous solution of ammonia (pH 11). The Ca/P ratio of the material increased with the latter treatment and the stoichiometric composition (Ca/P = 1.67) was achieved after six treatments. In contrast, essentially no change in composition was found with the former treatment. The treated powder had high thermal stability of nominally a stoichiometric composition. Composition change by incongruent dissolution is discussed.

1. Introduction

Hydroxyapatite ceramic is very promising for biomedical applications [1, 2]. The requirements for its ceramic raw powder are excellent powder characteristics and stoichiometric composition. To fulfil the former requirement, a wet process is generally favoured, and has been applied for the preparation of active hydroxyapatite powders [3–7]. Combined with a hot isostatic pressing technique, a powder synthesized and formed directly in a wet process produces a transparent material [8]. Great care is required in the stoichiometric control, however, in a wet process. The conditions needed to achieve the stoichiometric composition may not be compatible with those required for the best powder characteristics. For a precise control of stoichiometry, a dry process has been applied for the synthesis of powder [9]. This method may not be favourable for the preparation of powder with excellent powder characteristics.

This paper presents a new process which allows precise stoichiometric control in a wet process. The process consists of two steps, namely the precipitation of hydroxyapatite from reactant solution and the post-treatment for stoichiometric control. Independent control should be possible for each step, allowing wide freedom in the selection of processing parameters.

The basis of the post-treatment is incongruent dissolution of hydroxyapatite into an aqueous medium. Incongruent dissolution of hydroxyapatite in water has been reported for the stoichiometric composition [10–12], and was discussed in [11]. The dissolution of vanadium and fluorine hydroxyapatite has also been studied [13]. In the past incongruent dissolution was the main source of difficulty in stoichiometric control in wet powder synthesis.

In the first part of this study dissolution behaviour was examined for specimens with stoichiometric and non-stoichiometric compositions. This knowledge is essential for understanding the process, but has not previously been reported for non-stoichiometric composition. An understanding of the dissolution behaviour is also important for the application of the material, since the hydroxyapatite of human bone is known to be non-stoichiometric [14]. In the latter part of the study the stoichiometric control by the post-treatment is presented.

The thermal stability of the treated powder was also examined. Compositional variation may be present in each powder particle and may affect the thermal stability markedly [15, 16]. A stoichiometric hydroxyapatite is known to form oxyhydroxyapatite at high temperatures, but the crystal structure of hydroxyapatite is preserved up to 1673 K [17]. A non-stoichiometric hydroxyapatite forms tricalcium phosphate at 973 to 1073 K [16].

2. Experiment

2.1. Preparation of stoichiometric and non-stoichiometric hydroxyapatite

Dihydrogen ammonium phosphate aqueous solutions having two concentrations were prepared and added slowly to calcium nitrate solution to prepare hydroxyapatite having stoichiometric (SHAp, Ca/P = 1.67) and non-stoichiometric (DHAp, Ca/P = 1.60) compositions. The pH of both solutions were set to 11 by concentrated aqueous ammonia solution. After stirring and ageing for 24 h under continuous bubbling of argon, the product was washed four times with 4 litres of distilled water and dried at 373 K. To avoid composition change by washing, great care was taken to minimize the total amount of washing water.

2.2. Solubility of stoichiometric and non-stoichiometric hydroxyapatite

The specimen was placed into distilled water (pH 6.5) or a concentrated aqueous solution of ammonia (pH 11), stirred continuously for 72 h at 298 K and filtered. The specimen-to-water ratio was varied from

0957–4530/90 $03.00 + .12

TABLE I Calcium-to-phosphate ratio in reactants and products, and the specific surface area (SSA)

Sample	Ca/P (reactants)	Ca/P (products)	SSA ($m^2 g^{-1}$)
SHAp	1.68	1.67	127
DHAp	1.55	1.60	93

1 to $5 g l^{-1}$. The chemical compositions of both solid and liquid phases were determined as described below.

2.3. Analysis

Ethylenediaminetetraacetic acid back-titration was used for the analysis of calcium in the solid phase. To determine the calcium concentration in the liquid phase, atomic absorption spectroscopy (model AA-646, Shimazu, Japan) was used. The phosphate content was determined by photospectroscopic analysis using molybdenum vanadate. For the concentration regions below the detection limits of the above analysis methods, excess water was evaporated to concentrate the solutions. The specific surface area of the powder was determined by the BET method.

2.4. Composition control by alkali treatment

A batch of DHAp was divided into two parts. One part was added to distilled water (pH 6.5) and the other to the same amount of aqueous ammonia solution (pH 11). They were stirred for 10 h at 298 K and filtered. After small amounts of products were removed for sampling, they were subjected to another treatment. This procedure was repeated seven times.

2.5. Evaluation of the thermal stability

To evaluate the thermal stability, specimens were heated at a rate of $6 K min^{-1}$ to various temperatures, kept at these temperatures for 3 h and cooled to room temperature at a rate of $6 K min^{-1}$. The phases present were analysed with a powder X-ray diffractometer (Rigaku, 2023, Tokyo, Japan). The strongest diffraction peaks were used to estimate the amount of each phase present from the peak height; (2 1 1) for HAp, (4 4 1, 1 7 0) for α-tricalcium phosphate, and (2 1 7) for β-tricalcium phosphate.

3. Results

Table I summarizes the precipitation conditions and the characteristics of the powders. During the precipitation process, the pH of the solution decreased gradually from the initial value of 11 to 10 at the end of the precipitation process. The compositions of the starting mixture and precipitate were different. To prepare the stoichiometric powder (Ca/P = 1.67), the starting mixture must be adjusted to contain a slight excess of calcium (Ca/P = 1.68). From a starting mixture that was calcium deficient (Ca/P = 1.55), a powder with high calcium deficiency (Ca/P = 1.60) was obtained. Note, however, that the calcium deficiency in this powder was less significant than in the starting mixture. Mass balance of the system requires that the liquid phase be extremely phosphate rich at the end of the precipitation process under these conditions. These synthesized powders have high specific surface areas. The stoichiometric powder has a higher specific surface area than the non-stoichiometric powder.

Table II summarizes the results of solubility tests. In the dissolution of calcium, the pH of the aqueous medium has a marked effect. The total concentration of calcium ions in the liquid phase is approximately two orders of magnitude smaller at pH 11 than at pH 6.5, but the stoichiometry of the specimen did not affect the dissolution of calcium significantly. Dissolution of phosphate was affected markedly by both the pH of the solution and the stoichiometry of the powder. The concentration of phosphate in the liquid phase was markedly higher at pH 11 than at pH 6.5, and higher in DHAp than in SHAp. The accuracy of the analysis was reasonable. The compositions of powders determined by direct chemical analysis after the dissolution experiments were consistent with those calculated from the starting composition and the ions present in the solution.

Fig. 1 shows the change of the net Ca/P ratio in the DHAp after the treatment. At pH 11 the ratio increased almost linearly with the number of treatments, and reached 1.67 after six treatments. Further treatment had apparently no influence on the ratio. At pH 6.5 no detectable change was found in the ratio after these treatments.

Fig. 2 shows the effect of the Ca/P ratio on the thermal stability of the product, which was measured by the amounts of decomposition products, α- and β-tricalcium phosphates, relative to that of hydroxyapatite after heat treatment. For a given Ca/P ratio the relative amount of decomposition product increased with increasing temperature. For a given temperature the relative amount of decomposition product decreased with increasing Ca/P ratio; the thermal stability increased as the composition approached

TABLE II Solubility of stoichiometric and non-stoichiometric hydroxyapatite in an aqueous media having pH 6.5 and 11, and the Ca/P ratio in liquid and product as well as those calculated by the mass balance

Sample	pH	Sample/ liquid (g l)	[Ca] ($\times 10^5$ M)	[PO_4] ($\times 10^5$ M)	Ca/P (liquid)	Ca/P (product)	Ca/P (expected)
SHAp	6.5	1	7.70	2.46	3.13	1.67	1.66
SHAp	6.5	5	11.2	1.60	7.00	1.67	1.66
DHAp	6.5	1	9.60	9.63	1.00	1.60	1.61
DHAp	6.5	5	12.5	17.2	0.73	1.60	1.61
SHAp	11	1	0.12	5.66	0.02	1.67	1.68
SHAp	11	5	0.15	13.8	0.01	1.67	1.68
DHAp	11	1	0.21	13.0	0.02	1.65	1.63
DHAp	11	3	0.15	38.4	0.004	1.64	1.63
DHAp	11	5	0.15	58.8	0.003	1.64	1.63

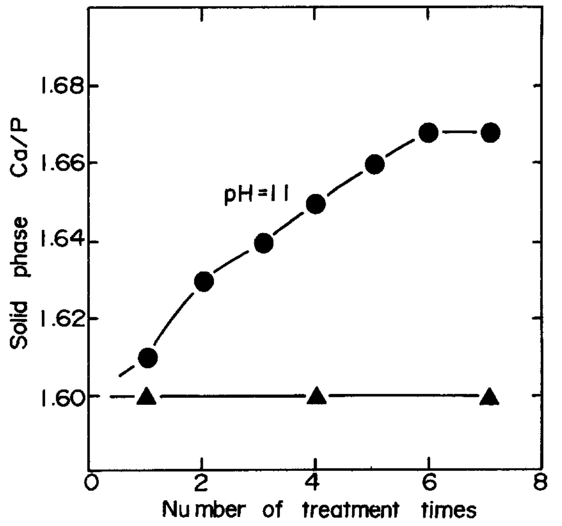

Figure 1 Change of the Ca/P ratio in the powder with treatment in an aqueous media having pH 6.5 and 11.

the stoichiometric one. Powder having nearly stoichiometric composition, Ca/P = 1.66, was stable up to 1573 K and decomposed slightly at 1673 K. This high thermal stability is comparable with that of the stoichiometric composition, for which no decomposition product was found after heating at 1673 K. Powder with a significant non-stoichiometry (Ca/P = 1.61) has very low thermal stability. A considerable decomposition has already started at 1073 K, which was the lowest temperature investigated. The amount of decomposition product increased significantly with increasing temperature.

4. Discussion

The decomposition temperatures of powders with various non-stoichiometric compositions in this study were approximately the same as in the previous studies reported for non-stoichiometric powders of similar compositions [15–17]. The stoichiometric composition prepared by the post-treatment has approximately the same thermal stability as the nominally stoichiometric composition. The preparation of stoichiometric composition with high thermal stability by the proposed process is a significant achievement, as explained above. We can optimize the powder characteristics freely without being affected by the restricting parameters which otherwise must be controlled to optimize the chemical composition. The result shows the great potential of the method in the development of excellent materials.

Incongruent solubility of hydroxyapatite is responsible for the stoichiometric change associated with the treatment [10–12]. It is also (at least partially) responsible for the difference in compositions between the starting mixture and the precipitate in powder synthesis.

In the present system a complicated relationship has been reported between the compositions in aqueous and solid phases, the pH of the aqueous phase and the relative amounts of solid and liquid phases [11]. However, for any given pH and solid-to-liquid ratio there must be a specific congruent composition for which Ca/P ratios in the solid and liquid phases are the same.

From results in Table II and Fig. 1 it is possible to estimate the approximate congruent compositions at pH 6.5 and 11. At pH 6.5 Table II shows that the Ca/P ratios in the liquid phase were, respectively, higher and lower than 1.67 for stoichiometric (Ca/P = 1.67) and non-stoichiometric (Ca/P = 1.60) powders. Clearly, a congruent composition at pH 6.5 is at a Ca/P ratio of between 1.60 and 1.67. Fig. 1 shows that this composition should be close to Ca/P = 1.60, since no measurable change of the Ca/P ratio was found after seven treatments at this pH for this powder. At pH 11 results of Table II and Fig. 1 again show that the composition for congruent dissolution should be at approximately Ca/P = 1.67 or even slightly higher.

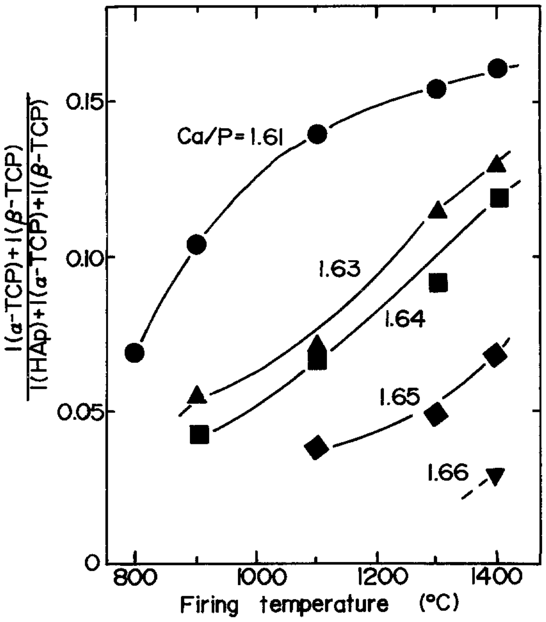

Figure 2 Effects of the Ca/P ratio and temperature on the amount of tricalcium phosphate formed by the thermal decomposition of hydroxyapatite. Firing time 3 h.

Incongruent dissolution can also explain the difference in compositions between the starting mixture and the precipitate found in the powder synthesis. In the preparation of stoichiometric composition, an excess calcium content (Ca/P = 1.68) was necessary in the starting mixture. At the end of powder synthesis at pH 10, if one recalls that the Ca/P ratio of the precipitate was 1.67, mass balance of the system requires that the Ca/P ratio in the solution which is in equilibrium with the stoichiometric precipitate must be significantly larger than 1.67. The result of Table I is consistent with this result; the pH at the end of this precipitation process (pH 10) was clearly too low to avoid the presence of excessive calcium ions in the solution. In contrast, the Ca/P ratio in the precipitate (Ca/P = 1.60) was much higher than in the starting mixture (Ca/P = 1.55) for the preparation of non-stoichiometric powder. Mass balance of the system requires that the liquid phase with Ca/P ratio significantly lower than 1.67 should be in equilibrium with the solid phase at the end of the precipitation process. This is again consistent with the results in Table II. For a product with Ca/P = 1.60 the equal compositions of the solid and liquid phases were possible only near pH 6.5. At pH 10 at the end of powder synthesis, the Ca/P ratio in the liquid phase over the solid (Ca/P = 1.60) should be significantly lower than 1.67, as found above.

Chemical processes of opposite direction are involved in precipitation and dissolution – the removal and the build-up of ions at the surface of solid. The same results in both precipitation and dissolution experiments show that the processes are very close to completion. The bulk of the powder should be close to equilibrium with the liquid phase.

It is easy to understand the result that the solid Ca/P ratio for congruent dissolution increases with increasing pH in aqueous medium. One must recall the general principle that the chemical potential of a constituent ion increases with its concentration in a non-stoichiometric compound [18]. In the lattice of hydroxyapatite, the phosphate sublattice is known to be rather defect-free [19]. Calcium vacancy should be responsible for calcium deficiency. With this defect model, the chemical potential of calcium relative to that of phosphate should increase with decreasing calcium deficiency (or with increasing solid Ca/P ratio). The solubility of calcium relative to that of phosphate at a given pH should also increase with increasing solid Ca/P ratio, which is consistent with the result in Table II. For the congruent dissolution of solid having a higher Ca/P ratio, consequently, a higher pH is needed to reduce the dissolution of calcium relative to phosphate.

The higher specific surface area in the stoichiometric powder than in the non-stoichiometric powder is consistent with the result reported by Asada *et al.* [7]. They prepared the powder with a starting Ca/P ratio of 1.48 to 1.80, and found that the specific surface area was quite constant for a ratio below 1.60 but increased with increasing ratio for a ratio above 1.60. They also found that the Ca/P ratio in the powder was quite constant (1.50) in the early period of reaction for all conditions, and that the unreacted calcium remained in the solution. They tentatively explained that the unreacted calcium ion and/or calcium hydroxide in the solution was responsible for the change of specific surface area with the Ca/P ratio.

The bulk composition of the post-treated powder is believed to be homogeneous in each powder particle, at least at the sintering temperature, since otherwise regions of non-stoichiometric composition must decompose at lower temperatures even in an apparently stoichiometric material.

There are two possibilities to achieve homogeneity at high temperatures. One is that the powder is homogeneous in the as-treated state, and the other is that the homogenization process occurs during the heating period. Since the chemical reaction during the post-treatment occurs only at the surface of the powder particles, a diffusion process must occur to form a homogeneous composition. Depending on the relative rate of surface reaction and the diffusion, there are two cases for the distribution of composition for the apparently equal net composition. One is the homogeneous powder particle, which requires a very rapid diffusion relative to the reaction rate at the surface. The other is the inhomogeneous powder, which requires just the opposite to be the case. Both are difficult to believe, but the former seems to be more probable. The very small particle size is clearly responsible for the formation of homogeneous composition during the powder synthesis. In general, the time needed for the completion of a diffusion process is inversely proportional to the square of the diffusion distance [21]. The temperature during the post-treatment in aqueous media is apparently very low to allow bulk mass transport of large scale in the solid phase, but is still sufficiently high to activate small-scale diffusion, which is needed in the present system. The ability of bulk ion-exchange of hydroxyapatite was reported in [20], and supports the above discussion. Further discussion of this problem requires a more detailed knowledge of the kinetics of these processes, and will be left for a subsequent study.

Acknowledgement

This work was supported by Grant in Aid for Scientific Research No. 01550591 from the Ministry of Education of Japan.

References

1. S. F. HULBERT, L. L. HENCH, D. FORBERS and L. S. BOWMAN, *Ceram. Int.* **8** (1982) 131.
2. M. AKAO, H. AOKI, K. KATO and A. SATO, *J. Mater. Sci.* **17** (1982) 343.
3. M. JARCHO, C. H. BOLEN, M. B. THOMAS, J. BOBICK, J. F. KAY and R. H. DOREMUS, *ibid.* **11** (1976) 2027.
4. J. ARENDS, J. CHRISTOFFERSEN, M. R. CHRISTOFFERSEN, H. ECKERT, B. O. FOWLER, J. C. HEUGHEBAERT, G. H. NANCOLLAS, J. P. YESINOWSKI and S. J. ZAWACKI, *J. Cryst. Growth* **84** (1987) 515.
5. T. KIJIMA and T. TSUTSUMI, *J. Amer. Ceram. Soc.* **62** (1979) 455.
6. T. FUTAGAMI and T. OKAMOTO, *Yogyo-Kyokai-Shi* **95** (1987) 775.
7. M. ASADA, K. OUKAMI, S. NAKAMURA and K. TAKAHASHI, *ibid.* **95** (1987) 781.
8. K. UEMATSU, M. TAKAGI, T. HONDA, N. UCHIDA and K. SAITO, *J. Amer. Ceram. Soc.* **72** (1989) 1476.
9. B. O. FOWLER, *Inorg. Chem* **13** (1974) 207.
10. G. L. LEVINSKAS and W. F. NEWMAN, *J. Phys. Chem.* **59** (1955) 164.
11. H. M. ROOTARE, V. R. DEITZ and F. G. CARPENTER, *J. Colloid Sci.* **17** (1962) 179.
12. A. CHUGHTAI, R. MARSHALL and G. H. NANCOLLAS, *J. Phys. Chem.* **72** (1968) 208.
13. S. K. GUPUTA, P. V. R. RAO, G. GEORGE and T. S. B. NARASARAJU, *J. Mater. Sci.* **22** (1987) 1286.
14. P. DUCHEYNE, *J. Biomed. Mater. Res.* **21** (1987) 219.
15. J. A. S. BETT, L. G. CHRISTNER and W. K. HALL, *J. Amer. Chem. Soc.* **68** (1967) 5535.
16. H. MONMA, *Gypsum Lime* (1980) 60.
17. T. KIJIMA and M. TSUTSUMI, *J. Amer. Ceram. Soc.* **62** (1979) 455.
18. O. T. SORENSEN, in "Nonstoichiometric Oxides", edited by O. T. Sorensen (Academic Press, New York, 1981) p. 2.
19. W. VAN RAEMDONCK, P. DUCHEYNE and P. DeMEESTER, in "Metal and Ceramic Biomaterials", Vol. II, edited by P. Ducheyne and G. W. Hastings (CRC Press, Boca Raton, Florida, 1984) p. 143.
20. M. MIYAKE, T. KOBAYASHI and T. SUZUKI, *Yogyo-Kyokai-Shi* **94** (1986) 832.
21. P. G. SHEWMON, "Diffusion in Solids" (McGraw-Hill, New York, 1963) p. 18.

Received 2 October
and accepted 8 November 1989