

A Study of a Biodegradable Inorganic-Organic Composite Artificial Bone Substitute

-Part 1. Synthesis of an Apatite with Similar Crystallinity to Bone-

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=Abstract=

To develop an artificial bone substitute that is gradually degraded and replaced by the regenerated natural bone, the authors designed a composite that consisted of calcium phosphate and collagen according to the natural bone's main composition. The crystallinity of the synthesized apatite was shown to depend on the synthesis temperature. Carbonate apatite synthesized at 58 °C demonstrated crystallinity very similar to that of the natural bone.

By sintering the apatite over 700 °C in vacuum, porous carbonate apatite could be obtained, and the pore extent was controllable according to the additive hydrogenperoxide volume.

Key words : Bone substitute, Crystallinity, Carbonate apatite

INTRODUCTION

Bone defects oriented from either extrinsic or intrinsic factors are usually restored by autograft or allograft in clinics. Restoration of the bone defect by xenograft or polymerized bone cement is also applied to the patients whose clinical conditions are limited to receive autograft or allograft. These bone replacing substitutes often reveal undesirable immunological reactions, therefore, many researchers have attempted to develop universal artificial bone substitute.

In recent, rapidly progressing ceramic engineering techniques have encouraged researchers to apply ceramic materials to biomedical materials. Calcium phosphate is a typical ceramic material that has attracted many researchers on its outstanding biostability and biocompatibility to bone. Hydroxyapatite(HAp) is the representative calcium phos-

phate ceramic that has been used in clinical practice since 1980s. Not only the easy producibility but also the synthesis condition-dependant varying controllable physical properties are advantages of the HAp. Implanted HAp surface is directly and chemically integrated to bone, and HAp exists as a bioinert mass with excellent biocompatibility. But it requires relatively long period to form complete bond to bone. Brittleness is also a no ignorable problem that limits HAp application to the physiological load unbearing area. Otherwise, tricalcium phosphate(TCP), another calcium phosphate that is replaced by bone after implantation, had been suggested to use as an artificial bone substitute. But in these days, TCP is not recommended by many orthopaedic surgeons due to its less compressive strength and accumulation of phosphate in the regional lymphnode.

To develop an artificial bone substitute that would be

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periodically degraded and replaced by natural bone after implantation, the authors designed a composite which consists of calcium phosphate, especially a carbonate apatite that comprises about 80% of the bone apatite, and collagen according to the main compositions of the natural bone. This paper covers a part of the research on synthesis of an inorganic substance, a carbonate apatite, that obtains similar crystallinity to the natural bone.

MATERIALS AND METHODS

1. Synthesis of apatite:

Calcium acetate solution (0.2 M) was supplied to ammonium acetate solution 1.3 M that is heated in a mantle heater with stirring at 260 rpm. Ammonium carbonate solution (0.06 M) and ammonium phosphate solution (0.12 M) were mixed, and also supplied to the ammonium acetate solution. The solution was controlled to pH 7.4 by adding NaOH solution. The synthesis was performed with varying temperatures at 98, 80, 60, 58, and 56 °C. The obtained apatite precipitates were dried at 60 °C in a dry chamber, and carbonate apatites were produced.

2. Sintering:

The obtained carbonate apatite powders synthesized at 58 °C were mixed with hydroxyperoxide solution at 88:12 in ratio of volume. Rods were produced by pouring the mixed pastes into a teflon mold with 3 cm of diameter and 5 cm of length. After drying the rods at 530 °C for 2 minutes, temperature was gradually increased by 20 °C per minute to 700 °C in vacuum of 70.0 cmHg. At 700 °C, the vacuum was released. The temperatures continued to increase to 700, 800, 900, 1000 and 1200 °C, and the rods were held at the final temperature for 2 minutes in a sintering furnace (Alphplus, Jelrus Co, USA).

3. Infrared spectroscopic analysis:

To investigate chemical compositions of the synthesized apatites, each 1mg of the carbonate apatite powder was mixed with 300 mg of KBr to prepare pellets. Peaks on wave length at 800~1600 cm⁻¹ were analyzed to confirm CO and PO bonds by an infrared spectrophotometer (Hitachi Perkin-Elmer 225 Grating Infrared Spectrophotomet-

er, Japan).

4. Crystallinity:

X-ray diffraction patterns of carbonate apatites were investigated. X-ray beam at 35kV and 23 mA was generated to a copper plate at 20~40 2θ° angles by an X-ray diffractometer (Rigaku Denki X-ray diffractometer, Japan). The peaks representing the apatite crystallinity at (002), (211), (112) and (300) were compared.

5. Electronmicroscopic observation:

Pore extent after sintering process was investigated by a scanning electron microscope (ABT DS-130C, JAPAN).

Carbonate apatite synthesized at 58 °C, that reveals similar crystallinity to the natural bone, was sintered at 700, 800, 900, 1000, and 1200 °C. The sintered specimens and the non-sintered one were observed.

RESULTS AND DISCUSSION

1. Synthesis temperature and acquired amounts of the carbonate apatite:

Carbonate apatite was synthesized by the modified procedures of Napper et al^{1, 2)}. The relationship between the precipitate amount and synthetic temperature were investigated. The reagent amounts were controlled to 500 ml of 1.3 M ammonium acetate solution, 250 ml of 0.2 M calcium acetate solution, each 125 ml of 0.06 M ammonium carbonate solution and 0.12 M ammonium phosphate solution. The synthesis temperatures were at 56, 58, 60, 80, 98 °C. The synthesized amount of the carbonate apatite was increased with increasing the synthesis temperature. Acquirable amounts of the apatite synthesized at 98 °C was about 1.32 times to that of the apatite synthesized at 56 °C (Fig. 1).

This result is similar to Okazaki's report in which the contents of the calcium and phosphate decrease with decreasing apatite synthesis temperatures²⁾.

2. Compressive strengths:

To simulate volume ratio of the inorganics and organics in the matured natural bone, the hydroxyperoxide, indicating the organics volume in bone, was mixed with carbon-

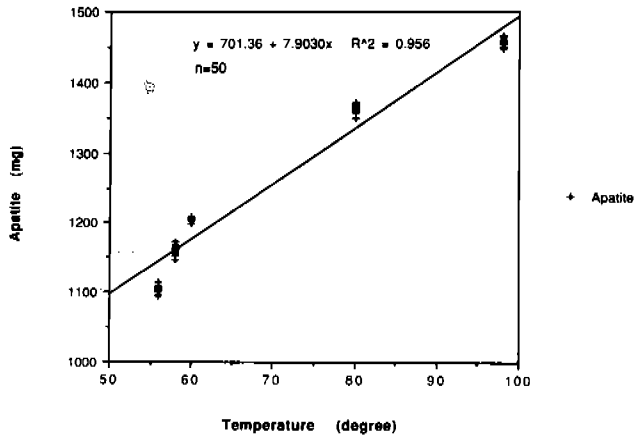


Fig. 1. Acquired amounts of carbonate apatite at various synthesis temperatures

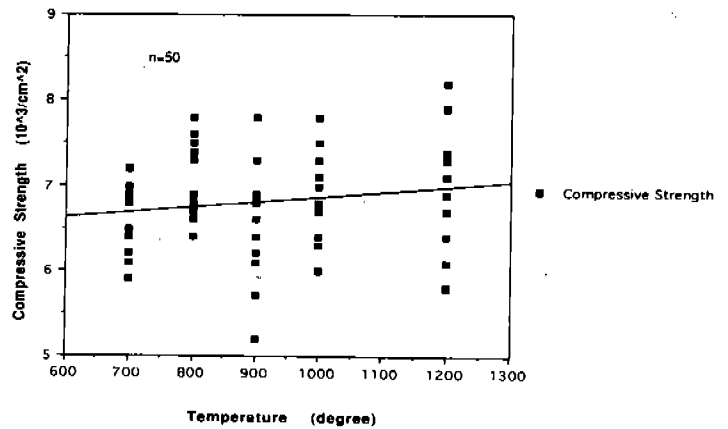


Fig. 2. Compressive strength depending on various sintering temperatures

ate apatite powders synthesized at 58 °C to 12:88 in volume ratio^{3, 4}). After sintering at various temperatures, compressive strengths were measured. Though the specimen sintered at 800 °C demonstrated some higher degree but there were no statistical differences (Fig. 2). It may be concerned that the stronger fusion on the apatite grain boundaries would be accompanied by increasing sintering temperature, and the hardness increases. But the increased sintering temperature also results in the increased brittleness, a typical characteristics of the ceramics, that leads to the less resistance to the compressive strength^{5, 6}).

To evaluate all the data of experiment 1) and 2), the Linear Regression was chosen as a statistically optimal analysis method. In this study, "p" value, which indicates that whether the linear regression method is a suitable method to treat the data for the study, was 0.025. Direct linear correlation is noted as "y" value, and was $701.36 + 7.90 \times$ in the experiment 1). "r²" indicates that how much data are gathered around the line.

3. Carbonate content in the apatite :

In the infrared spectroscopic analysis, the wave lengths on 1410 and 1460 cm^{-1} represent CO_3^{2-} ion concentration, and 960 cm^{-1} indicates PO_4^{3-} ion concentration, respectively. On carbonate apatite synthesis, the increasing carbonate content results in the notably decreased phosphate content but less decreased calcium content⁷). In this study, only the

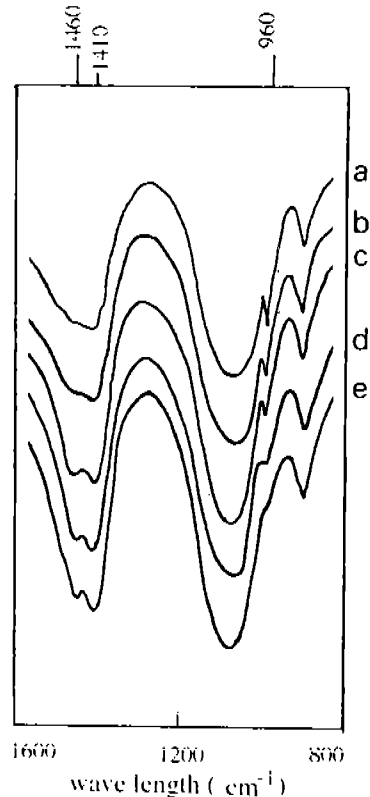


Fig. 3. Infrared spectroscopic intensities depending on synthesis temperatures (a) 98 °C, (b) 80 °C, (c) 60 °C, (d) 58 °C, (e) 56 °C

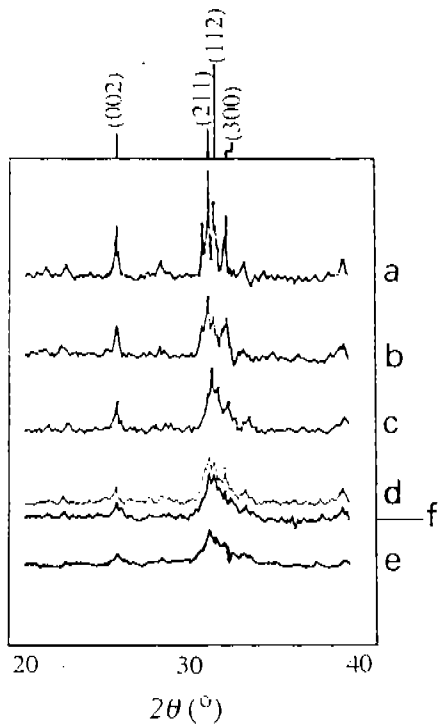


Fig. 4. X-ray diffraction patterns depending on synthesis temperatures (a) 98 °C, (b) 80 °C, (c) 60 °C, (d) 58 °C, (e) 56 °C, (f) bone

synthesis temperature was varied with that of same reagents' amounts. The carbonate content decreased following to the increased synthesis temperature. The contents of calcium and phosphate decreased according to the decreased synthesis temperature (Fig. 3). This result can be related to the result of the less acquired carbonate apatite amount at the lower synthesis temperature.

4. Crystallinity of the carbonate apatite :

To compare the crystallinities of the carbonate apatites with synthesis temperatures, X-ray diffraction patterns were investigated on the apatites synthesized at 56, 58, 60, 80 and 98 °C. The intensity of the carbonate apatite synthesized at 58 °C demonstrated nearly similar pattern to that of the matured natural bone at (002), (211), (112) and (300) (Fig. 4). This result reveals that a carbonate apatite, with the more similar crystallinity to bone than that of the author's former report, was obtained⁸⁾.

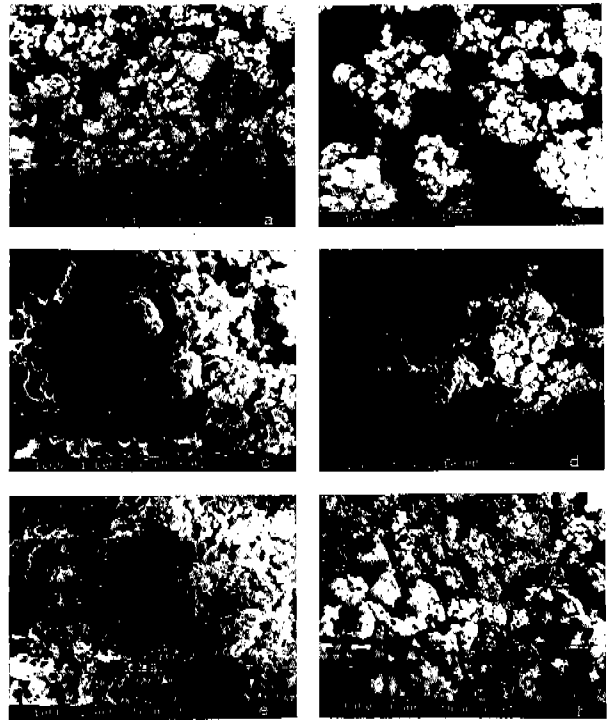


Fig. 5. Scanning Electron Microscopic views of the sintered carbonate apatites (a) non sintered, (b) 700 °C, (c) 800 °C, (d) 900 °C, (e) 1000 °C, (f) 1200 °C

5. Porosity after sintering :

There were no significant differences in formation of the porosity extents in the specimens of various synthesis temperatures such as non-sintered or sintered at 700, 800, 900 and 1000 °C (Fig. 5). This result demonstrates that the porosity formation depends on the volume of the mixed hydroxyperoxide but not on the sintering temperature.

CONCLUSION

A carbonate apatite with similar crystallinity to the natural bone was synthesized to use as an artificial bone substitute, which would be degraded and replaced by the regenerating bone after implantation into bone defects. The following results could be obtained :

1. Increasing synthesis temperature produces the more amount of apatite precipitate but less amount of car-

bonate apatite.

2. A carbonate synthesized at 58 °C demonstrated a nearly similar crystallinity to the natural bone.
3. Porosity extent is not related to the sintering temperatures but depends on the quantity of the mixed hydroxyperoxide.

ACKNOWLEDGMENT

The authors appreciate Mr. Soo-Won Suh and Young-Joo Park, Miss Sue-Jin Ahn and Jin-Ja Park for their diligent assistances on proceeding this study.

This research has been supported by the Korea Science and Engineering Foundation. (Grant No. 93-13-00-01-3)

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