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Porous Composite of Magnetite / Apatite with Bimodal Pore Size Distribution

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Porous composites of magnetite / hydroxyapatite with bimodal pore size distribution were prepared by hydrothermal method at 120 °C under the saturated vapor pressure for 10 h. Magnetite particles of about 1 μm in size with polyhedral shape were dispersed into hydroxyapatite porous matrix. The hydroxyapatite particles were rod-shaped crystals and the size of crystals were about 10 μm in length with the aspect ratio of over 25. Rod-shaped hydroxyapatite crystals were locked together to make micro-pores less than 500 nm in size. In addition, macro-pores of about 400 μm in size were prepared by our unique method. HA in this composite was non-stoichiometric hydroxyapatite with calcium deficient composition. This composite must have the advantage of adsorptive activity and osteoconductivity, because the hydroxyapatite has many specific crystal surface and micro-pores. Microstructure designed composites of magnetite / hydroxyapatite must be suitable for the hyperthermia therapy of cancer in bones.

Key words: Hydroxyapatite, Hydrothermal, Porous Composite, Hyperthermia, Biomaterial

1. INTRODUCTION

Hydrothermal processing plays a key role in the preparation of ceramic biomaterials with biocompatibility in the physiological environment [1]. The present study deals with the preparation of porous composite for medical treatment. Hyperthermia is a new therapy of cancer that based on the cell activity at high temperature of about 43 °C to 48 °C. Cancer cells are destroyed when they are heated up to about 43 °C, and that is only 6 °C above the normal body temperature, whereas normal cells are not damaged up to 48 °C. In addition, a tumour is preferentially heated, as nerve and blood systems are not fully developed in a tumour. Therefore, hyperthermia therapy can also be an effective non-invasive treatment for cancer. There are some kinds of method in hyperthermia, they are supersonic-therapy, hot-water-therapy and infrared radiation-therapy. These methods heat not only cancer cells but also normal cells, because it is difficult to heat deep-seated cancers both effectively and locally. The normal tissue near to the surface of the body should be damaged, therefore we need to find a new method which can heat only a carcinomatous area [2-10].

Gilchrist et al. suggested some idea to make effective use of the property of ferrite for hyperthermia [11]. If ferrite is accumulated only in the carcinomatous area, it can heat and it can kill cancer cells effectively. Specific heating for cancer cells is available, because ferrite generates heat by hysteresis loss under a high frequency magnetic field. To embed ferrite in the tumour of bones, porous hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$: HA) composites with magnetite (Fe3O4) dispersion should be suitable, because HA was one of the most biocompatible materials with human bones and HA can bond to bones directly [13, 14].

This study presents a new solution to establish a highly ordered Fe_3O_4 / HA porous composite composed of rod-shaped particles of HA with Fe_3O_4 particles dispersion. Microstructure designed composites of Fe_3O_4 / HA must be suitable for the hyperthermia therapy for bones.

2. EXPERIMENTAL METHODS

2.1 Pure hydroxyapatite ceramics

Commercial powders of α-tricalcium phosphate (α-$Ca_3(PO_4)_2$: α-TCP, Taihei Chemical Industrial Co., Ltd., Japan) were used as the starting material. α-TCP powder was molded with water addition into cylindrical shape of 8 mmϕ × 1 mmL under about 10 MPa compression. Cylindrical samples were set in a 105 cm^3 autoclave (Figure 1) with 10 cm^3 of water, then they were exposed to vapor of the solution at 120 °C under saturated vapor pressure for 10 h. Next, samples were retreated hydrothermally in the liquid phase at 200 °C for 10 h in water or NH_3 aq. of pH 11.

2.2 Composite of magnetite / hydroxyapatite

Preparation method of composites is shown in Figure 2. Commercial powders of α-TCP and magnetite (Fe_3O_4 : Wako Chemical Co., Japan) were used as the starting material. After the addition of 30 vol% Fe_3O_4 particles of about 1 μm in size to α-TCP, the mixed powder was molded with water addition into cylindrical shape of 8 mmϕ × 1 mmL with PLLA fiber of 400 μmϕ. After molding, PLLA fiber was pulled out to make interconnecting macro-pores. The composite materials of Fe_3O_4 / α-TCP were set in a 105 cm^3 autoclave (Figure 2) with 10 cm^3 of water, then they were exposed to vapor of water at 120 °C under saturated vapor pressure for 10 h. Then the samples were retreated hydrothermally in the liquid phase at 200 °C for 10 h in water or NH_3 aq. of pH 11.

The produced phases were identified by powder X-ray diffractometry with graphite-monochromatized CuKα radiation, operating at 40 kV and 20 mA (XRD; Mac Science, MXP^3, Japan). The microstructure of specimens was observed by scanning electron microscope for the surface and for the fractured surface (SEM; JEOL, JSM-T300, Japan). Magnetization curves of composites were measured by vibrating sample

magnetometer (VSM ; Tamagawaseisakusyo, TM-VSM 1230-HHHS).

3. RESULTS AND DISCUSSION

3.1 Pure hydroxyapatite ceramics

α-TCP changed into HA with a little amount of β-tricalcium phosphate (β-$Ca_3(PO_4)_2$: β-TCP) by hydrothermal vapor exposure treatment. Both HA and β-TCP has good biocompatibility, but solubility of β-TCP was higher than that of HA in body fluid [15]. When the composite of Fe3O4 / HA with β-TCP will be implanted in the affected part, β-TCP will dissolve and then Fe3O4 particles will be released. Therefore, pure HA without β-TCP is required. On the other hand, the sample prepared by the soaking treatment after the vapor exposure method has only HA. By using hydrothermal soaking method, β–TCP, as the impunity, changed into HA completely.

The surface of samples was composed of rod-shaped particles. Micro-pores less than 500 nm were made by tangle of them. After using hydrothermal soaking method, rod-shaped HA particles were remained.

Therefore, in order to obtain pure crystal phase of HA and HA rod-shaped particles with large aspect ratio, the soaking treatment after the vapor exposure method was required.

3.2 Composite of magnetite / hydroxyapatite

Porous composites of Fe3O4 / HA can not be prepared by sintering method at high temperature. Because Fe3O4 is stable at the temperature below about 300 °C and decomposed into hematite at the temperature over about 300 °C. On the other hand, hydrothermal method using relatively low temperature could make HA easily and could make no change of Fe3O4.

According to XRD measurement, samples prepared by hydrothermal soaking method were no other phases than HA and Fe3O4 (Fig. 3). Fe3O4 did not affect the hydration of α-TCP.

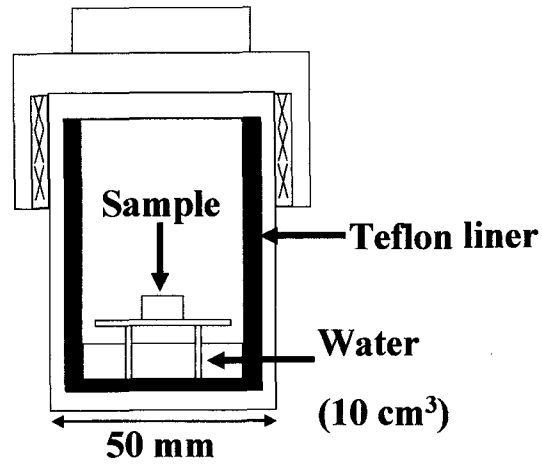

Fig.1 Schematic illustration of apparatus for hydrothermal treatment.

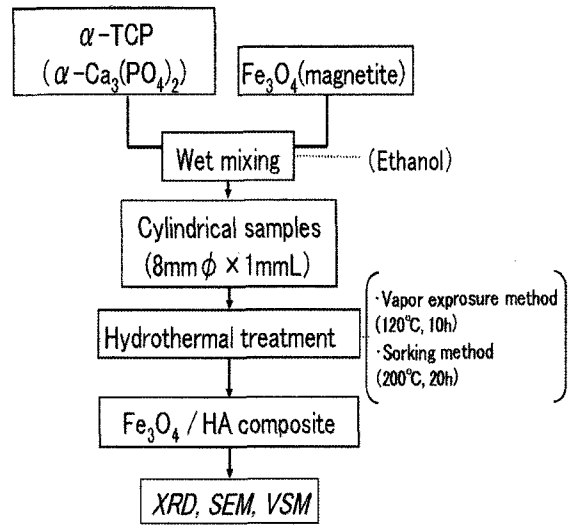

Fig.2 Preparation method of porous composites of magnetite / hydroxyapatite.

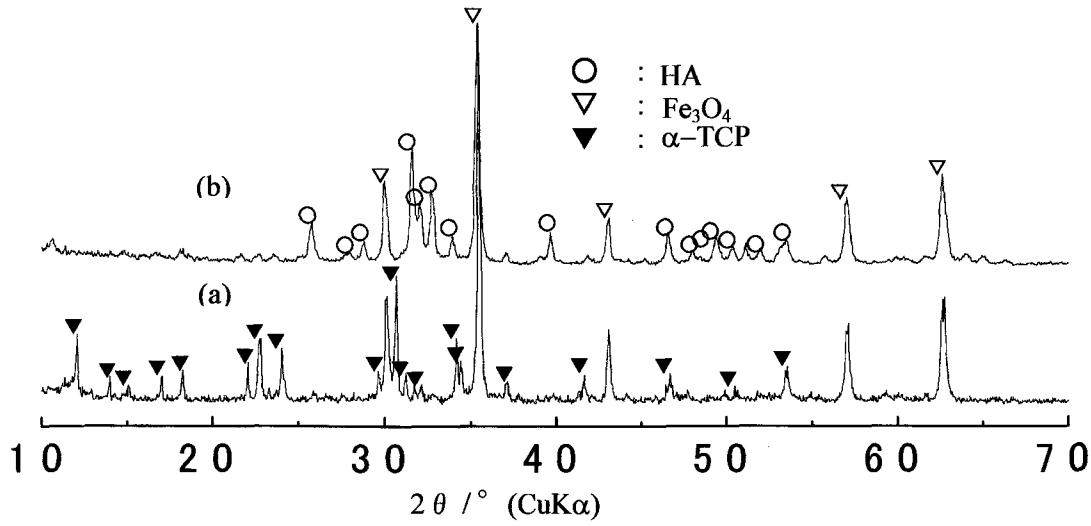

Fig.3 XRD patterns of (a) starting mixture of α-TCP and Fe_3O_4, (b) the composite prepared by hydrothermal method. The sample (b) was first treated hydrothermally in the vapor of water at 120 °C for 10h, and secondly treated hydrothermally in the liquid phase at 200 °C for 10h.

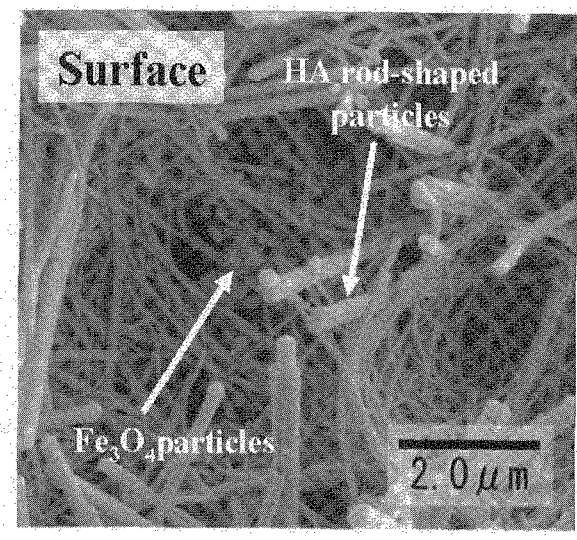

Fig.4 SEM photograph of the surface of 30 vol% magnetite / 70 vol% hydroxyapatite composite prepared by hydrothermal method.

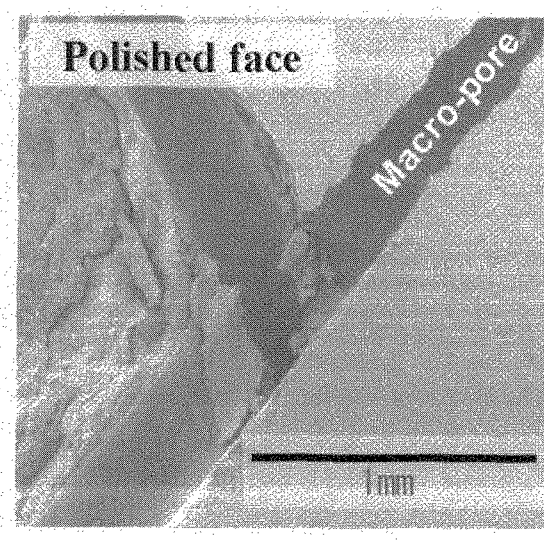

Fig.5 SEM photograph of the polished face of 30 vol% magnetite / 70 vol% hydroxyapatite composite prepared by hydrothermal method. Macro-pore was observed.

Figure 4 shows the surface of the composites with 30 vol% Fe_3O_4 particles prepared by hydrothermal treatment, and figure 5 shows the polished face of the composite. The surface of composite was composed of rod-shaped crystals elongated along the c-axis of about 10 μm in length with the mean aspect ratio over 25. Rod-shaped crystals were locked together to make micro-pores, and the size of micro-pores formed by tangle of HA rod-shaped particles was below 500 nm by SEM observation. So Fe3O4 particles of about 1 μm in size with polyhedral shape were held into HA porous matrix. Micro-pores must be suitable for adhering proteins for promoting cell activities. In addition, the composite prepared by hydrothermal treatment had interconnecting macro-pores with the diameter of about 400 μm in size. Macro-pores must be suitable for cell penetration and cell activities.

The porosity of the composite was about 68 %. For bone formation, the composite should have many pores and high porosity. But too much higher porosity makes the mechanical strength lower. Therefore, porosity control between 60 % and 70 % is required for clinical applications. This composite must have the good biocompatibility and must bond to the natural bone [1].

Figure 6 shows the magnetization curve of the composite of 30 vol% Fe3O4 / 70 vol% HA under a magnetic field up to 300 Oe. The saturation magnetization and coercive force of the samples were 1.56 emu and 95 Oe respectively. When these composites were used under 300 Oe and 100 kHz, we calculated the calorific value of this composite, about 1.1 W. Thus the composites can be a promising candidate of thermo-seeds for effective hyperthermia.

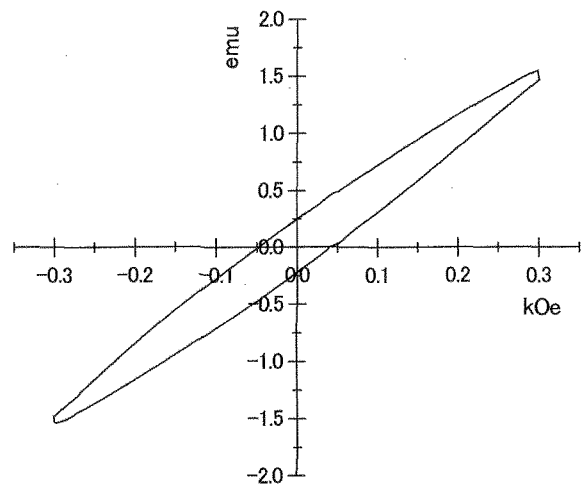

Fig.6 Magnetization curves under the magnetic field up to 300 Oe for the 30 vol% magnetite / 70 vol% hydroxyapatite composite prepared by hydrothermal method.

4. CONCLUSIONS

Microstructure designed magnetite (Fe_3O_4) / hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) porous composites were prepared by hydrothermal method. These composites must have the advantage of adsorptive activity and bone generation, because the HA has many specific crystal surface, micro-pores and macro-pores for cell activity. In this method, these composites have both properties of HA and Fe3O4, therefore microstructure designed composite of magnetite / hydroxyapatite must be suitable for hyperthermia therapies of cancer in bones.

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