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Biocompatibility of Apatite-Containing Implant Materials

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Abstract—Thermochemical decomposition of hydroxyapatite in phosphoric acid was studied with the aim of producing polymineral gradient-resorptivity composites. The procedure was tested on the BAK-1000 glass–apatite composite. The results indicate an enhancement of resorptivity, without changes in the performance parameters or crystal structure, thereby suggesting a new approach to controlling the bioactivity of apatite-containing bioceramics.

INTRODUCTION

Materials based on hydroxyapatite (HA), $Ca_{10}(PO_4)_6(OH)_2$, are the most widely used inorganic biomaterials, because HA is closely similar in chemical composition, structure, and physicochemical properties to the mineral component of an osseous tissue and possesses unique biomimetic properties. A major drawback of all HA-based materials is their low resorptivity in physiological solutions with pH 7.3. This is characteristic even for materials prepared at temperatures below that of the transition to a crystalline condensed form with a high degree of structural ordering and low resorptivity.

The main lines of research concerned with the preparation of apatite-containing biomaterials with controlled bioactivity are as follows:

(1) Preparation of nonstoichiometric HA and determination of its stability conditions;

(2) Modification of the HA structure with foreign ions;

(3) Design of polymineral composites incorporating HA and calcium phosphates.

In the first two instances, resorptivity depends on the structural perfection of HA: nonstoichiometry, type of solid solutions, site occupancies, and distribution of the effective charge in the presence of foreign cations. As for the third line of research, note that the most common component of composites with HA is tricalcium β-phosphate (TCP)—the only phosphate which fully resorbs in human tissue, whereas other phosphates experience weak resorption and belong to the class of resistive compounds [1–4]. There is some evidence that TCP-based implants resorb more rapidly than do HA-based implants [5, 6]. Jarcho [7] points out that the resorption rate of implants is proportional to the TCP content: increasing the fraction of HA reduces the resorption rate.

These observations are consistent with the physicochemical characteristics of these compounds in solution: the solubility of TCP is one order of magnitude higher than that of HA [8]. The solubility of HA is immeasurably low in pure water (dissociation constant, 10^{-100} [9]) but depends strongly on solution pH. The presence of TCP increases the ionic strength of the solution, changing the pH and raising the HA solubility.

β-TCP can be introduced in a number of ways; direct sintering of mechanical mixtures of HA and β-TCP is not used. In some cases, it is expedient to synthesize HA with the desired β-TCP content by solid-state reaction. In most instances, however, use is made of chemical treatment or partial thermal decomposition of HA. Certain chemical reagents were found to yield granules in which a HA core is sheathed by β-TCP. For example, Berger *et al.* [10, 11] treated HA with solutions of phosphoric and sulfuric acids or a mixture of phosphoric, sulfuric, and hydrofluoric acids and then heat-treated it. The well-known material Interpore 500 also contains β-TCP and can be prepared by reacting the carbonate skeleton of coral with $(NH_4)_2HPO_4$ and H_3PO_4 solutions [12]. To prepare gradient ceramics, with the mineral composition varying with depth, diamond powder is applied to an HA workpiece before firing. Burning of the powder leads to HA decomposition into TCP on the surface [13].

TCP may also result from the reactions accompanying sintering of HA. The polycrystalline ceramics fabricated by Osborn [14] contained 70–95% rutile, HA, and TCP, which results from the decomposition of HA powder in the range 1200–1300°C and is present in the form of a grain-boundary phase.

Yoshio *et al.* [15] produced high-porosity ceramics, with the skeleton built from long TCP fibers, by sintering the products of acidic leaching of $46CaO \cdot 54P_2O_5$ ultraphosphate glass.

The objective of this work was to study the thermochemical decomposition of stoichiometric HA into β-TCP. This process might offer a means of controlling the bioactivity of apatite-containing implant materials

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via the production of polymineral composites incorporating calcium phosphates with different solubilities.

EXPERIMENTAL

HA was synthesized in aqueous solutions by neutralizing calcium hydroxide (analytical grade) with phosphoric acid (extrapure grade) at 100°C. The HA powders thus prepared were heat-treated in a muffle furnace, where temperature was maintained semi-automatically. Phase composition of the resulting materials was determined by qualitative x-ray diffraction (XRD) analysis (DRON-3M diffractometer, CuK_α radiation, scan rate of 1°(2θ)/min). The β-CTP content of the material was determined by quantitative XRD analysis using mixtures of HA and β-TCP for calibration. The weight fraction of β-TCP was evaluated from the intensity of the peaks with d = 2.8139 Å for HA (ASTM, 9-432) and d = 2.8669 Å for β-TCP (ASTM, 9-169) using the calibration plot of intensity vs. weight percent of β-TCP. IR absorption spectra were measured between 400 and 4000 cm^{-1} on a Specord 75 IR spectrophotometer using powder samples with an isopropanol binder. The resorptivity of the materials was evaluated before and after thermochemical processing from weight loss data for 10-cm^3 samples in a 0.6 N HCl solution (USSR State Standard GOST 3118-77).

RESULTS AND DISCUSSION

HA was obtained in the form of a readily agglomerating white powder with a specific surface of 70 m^2/g. The size of individual needlelike crystallites was no greater than 4 μm. According to chemical analysis and IR absorption data (Fig. 1, spectrum *1*), the Ca/P atomic ratio in the synthesized HA was 1.67. The XRD pattern contained only reflections from HA, indicating that the material was phase-pure.

In choosing the reagent for chemical treatment of HA with the aim of obtaining calcium phosphates with Ca/P < 1.67, we took into account the following:

The compound must contain monophosphate or phosphorus ions.

The reagent should not contain Ca in order not to increase the Ca/P ratio.

The reagent must be volatile and readily soluble in water.

The product of reaction between the reagent and HA must be biocompatible and consist only of HA and β-TCP.

All these requirements are fulfilled by phosphoric acid. The phase compositions of the products obtained by treating HA with phosphoric acid, followed by heat treatment at different temperatures, are listed in Table 1.

At room temperature, HA reacts with phosphoric acid to form acid calcium monophosphate hydrate (brushite), which looses water of crystallization starting at 25°C. The presence of hydrophosphate groups is evidenced by the prominent absorption at 875 cm^{-1}, which can be assigned to vibrations of the HPO_4^{2-} group (Fig. 1, spectrum *2*) [16]. Increasing the temperature to 500°C gives rise to disproportionation reactions—proton transfer between neighboring phosphate groups, without rearrangement of ions in the crystal lattice:

$$3HPO_4^{2-} \longrightarrow 2PO_4^{3-} + H_3PO_4.$$

This process seems to be reversible, so that there is a certain equilibrium between different phosphate spe-

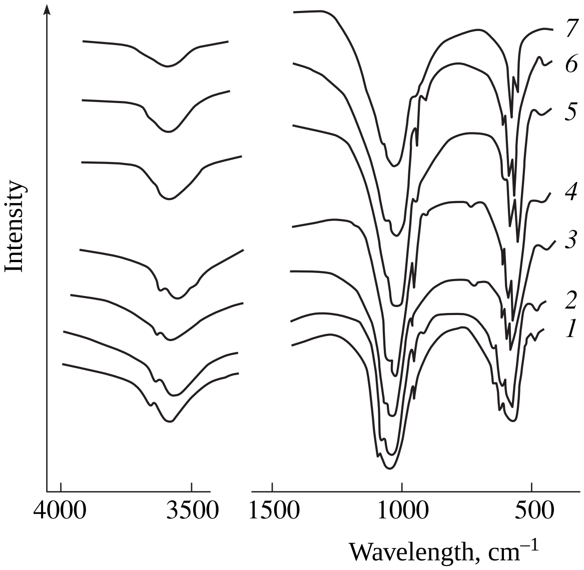

Fig. 1. IR spectra of HA (*1*) before and (*2*–*7*) after reaction with H_3PO_4 and heat treatment for 1 h at (*2*) 200, (*3*) 500, (*4*) 700, (*5*) 900, (*6*) 1000, and (*7*) 1200°C.

Table 1. Phase composition of the products obtained by thermochemical processing of HA in phosphoric acid (XRD data)

t, °C	Phase composition
20	$Ca_{10}(PO_4)_6(OH)_2$, $CaHPO_4 \cdot 2H_2O$
200	$Ca_{10}(PO_4)_6(OH)_2$, $CaHPO_4$
500	$Ca_{10}(PO_4)_6(OH)_2$, γ-$Ca_2P_2O_7$
700	$Ca_{10}(PO_4)_6(OH)_2$, γ-$Ca_2P_2O_7$, β-$Ca_3(PO_4)_2$
800	$Ca_{10}(PO_4)_6(OH)_2$, β-$Ca_2P_2O_7$, β-$Ca_3(PO_4)_2$
850	$Ca_{10}(PO_4)_6(OH)_2$, β-$Ca_3(PO_4)_2$
900	$Ca_{10}(PO_4)_6(OH)_2$, β-$Ca_3(PO_4)_2$
950	β-$Ca_3(PO_4)_2$
1200	α-$Ca_3(PO_4)_2$

Note: The concentration of the H_3PO_4 solution corresponded to a Ca/P atomic ratio of 1.5. Reaction was run for 1 h.

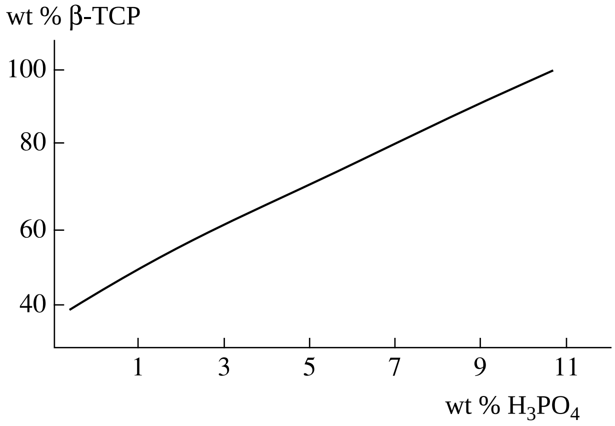

Fig. 2. Content of β-TCP after thermochemical processing of HA in different H_3PO_4 solutions at 900°C.

cies, dominated by the one which lies at the basis of the HA structure. The HPO_4^- groups can be thought of as structural defects. Heating to 500°C gives rise to condensation of the HPO_4^{2-} groups into diphosphate groups, as evidenced by the feature at 720 cm^{-1} in the IR spectrum (Fig. 1, spectrum *3*). The disappearance of this feature and the OH^- stretching band (3560 cm^{-1}) upon heating to 800°C (Fig. 1, spectra *3*–*5*) suggests that, in the range 500–800°C, $P_2O_7^{4-}$ groups react with hydroxyls:

$$P_2O_7^{4-} + 2OH^- \longrightarrow 2PO_4^{3-} + H_2O\uparrow.$$

In the range 850–900°C, the content of HA and β-TCP after 1 h of reaction is fairly low, 45–50 wt %. The yield of the reaction between HA and phosphoric acid can be fine-tuned by adjusting the reagent concentrations (Fig. 2).

Table 2. Properties of the BAK-1000 implant material

Characteristic	Before processing	After processing
Phase composition, wt %		
Glass	50	50
HA	50	25
β-TCP	–	25
Resorption in 0.6 N HCl at 20°C in 24 h, wt %	22	40
Porosity, %	58	55
Flexural strength, MPa	9.3	9.5
Bulk density, kg/m^3	1000	1070

The thermochemical method was tested on an apatite-containing composite with the BAK-1000 silicate matrix, which is used in plastic surgery [17]. The properties of this material before and after thermochemical processing in a solution of phosphoric acid are listed in Table 2.

The reaction between HA and phosphoric acid involves chemical and polymorphic transformations of calcium phosphates in the range 20–900°C. The characteristic features of this process correlate with earlier results [18]. The absence of β-TCP among the products of reaction at room temperature indicates the necessity of heat treatment.

The low-temperature form of TCP is observed starting at 700°C. Two-phase materials, comprising only HA and β-TCP, can be obtained in a narrow temperature range, between 850 and 900°C. Above 900°C, the only reaction product is β-TCP (Fig. 1, spectrum *6*), which transforms into the α-form at 1200°C (Fig. 1, spectrum *7*).

CONCLUSION

The temperature range in which two-phase materials consisting of HA and β-TCP can be prepared is fairly narrow, from 850 to 900°C. The major parameter for controlling the relative amounts of HA and β-TCP in this temperature range is the HA/H_3PO_4 ratio in the reaction system.

As distinct from the thermal decomposition of stoichiometric HA, thermochemical processing allows two-phase composites to be prepared below 1000°C. By varying the concentration of phosphoric acid, one can obtain materials containing 40–100 wt % β-TCP and also gradient ceramics in which the composition varies from HA to β-TCP across the implant or from the center to the surface of the granule.

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