# **BIOMATERIALS**

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## **COMPOSITE CERAMIC CONTAINING A BIORESORBABLE PHASE**

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The production of a multiphase ceramic in the system  $\text{CaO} - \text{P}_2\text{O}_5$  from mixtures of powders of hydroxyapatite and monetite, synthesized from calcium nitrate and ammonium hydrophosphate, is investigated. Monetite CaHPO<sub>4</sub> is used as the source of the resorbable phase of the composite ceramic — calcium pyrophosphate. It is established that a solid-phase reaction in which hydroxyapatite and calcium pyrophosphate interact to form tricalcium phosphate occurs during calcination.

A worldwide search is now underway for materials which are suitable for introducing into the human body for purposes of diagnostics, medical treatment, or replacement of bone tissue. Physicians are especially interested in ceramic materials whose chemical composition is close to that of natural bone tissue. This is a ceramic based on calcium-phosphate compounds, primarily hydroxyapatite (HAP) — a material which is identical to the biomineral of human bones. Together with biocompatibility and bioactivity, materials for bone implants must exhibit bioresistance (resistance to dissolution in the body) or bioresorbability (capability of gradually or completely dissolving in water in the body as the new bone accumulates) depending on the medical treatment being used.

A material containing a 100% HAP phase has the highest bioresistance [1]. To regulate the level of bioresistance (biodegradability) the material must contain a bioresorbable phase in addition to the bioresistive phase HAP. The best studied materials are those which contain as the resorbable phase tricalcium phosphate (TCP) or CaO - P<sub>2</sub>O<sub>5</sub> - M<sub>2</sub>O and  $CaO - P_2O_5 - SiO_2 - M_2O$  (M — Na, R) glasses [2, 3]. Ceramic materials containing phase calcium pyrophosphate (CPP) as the resorbable have not, for all practical purposes, been studied. One reason that materials containing CPP have been excluded from studies could be the fact that CPP is present in the joints of people suffering from arthritis and arthroses. Nonetheless, the pyrophosphate ion is the main structural unit of biphosphonates [4], which are the base of many pharmaceuticals for treating osteoporosis and diabetes mellitus [5].

HAP and some other complex phosphates are the final products of the biological mineralization process, and  $\beta$ -CPP is one of the intermediate products in this process. As reported in [6], sintered  $\beta$ -CPP promotes bone-cell formation better than does HAP.

Pyrophosphate ions are strong inhibitors of the crystallization of calcium phosphates, and feedback between alkaline phophatases and membrane plasmatic glycoproteins regulates their level *in vivo*. This regulation process is considered to be very important for mineralization of bone [7].

Pyro- and polyphosphate ions participate in the regulation of many important biological processes. Polyphosphate ions are present in many tissues throughout the entire body, but they are most highly concentrated in osteoblasts. The high content of exopolyphosphatases, which split the orthophosphate ions off polyphosphate compounds, in osteoblast cells indicates that polyphosphate ions have a large effect on the formation and growth of bone mineral [6].

CPP can crystallize from glasses of the system  $CaO - P_2O_5$  or form from brushite via monetite on heating.

#### Transformation of brushite on heating in air [2]

Transformation	Transformation temperature, °C
$CaHPO_4\cdot 2H_2O \rightarrow CaHPO_4. \ . \ . \ .$	60 – 100 (in solution or with prolonged
	storage in air)
$CaHPO_4 \rightarrow \gamma\text{-}Ca_2P_2O_7  .  .  .  .$	
$\gamma$ -Ca <sub>2</sub> P <sub>2</sub> O <sub>7</sub> $\rightarrow \beta$ -Ca <sub>2</sub> P <sub>2</sub> O <sub>7</sub>	500 – 750
$\beta$ -Ca <sub>2</sub> P <sub>2</sub> O <sub>7</sub> $\rightarrow \alpha$ -Ca <sub>2</sub> P <sub>2</sub> O <sub>7</sub>	1165

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Fig. 1. Crystal structure of  $\beta$ -Ca<sub>2</sub>P<sub>2</sub>O<sub>7</sub> (*a*) and  $\alpha$ -Ca<sub>2</sub>P<sub>2</sub>O<sub>7</sub> (*b*) [7].

CPP has the same structure as potassium dichromate. The lattice parameters of  $\beta$ -CPP and  $\alpha$ -CPP [8] are presented in Table 1 and their crystal structure is shown in Fig. 1.

There are three modifications of CPP, of which  $\beta$ -Ca<sub>2</sub>P<sub>2</sub>O<sub>7</sub> is tetragonal and  $\alpha$ -Ca<sub>2</sub>P<sub>2</sub>O<sub>7</sub> is monoclinic. Condensation of orthophosphate ions results in the formation of pyro- and polyphosphate ions. Each of the two PO<sub>4</sub> groups in CPP is a strongly screened configuration with P – O – P angles equal to 131 and 138° for  $\beta$ -Ca<sub>2</sub>P<sub>2</sub>O<sub>7</sub> and 130° for  $\alpha$ -Ca<sub>2</sub>P<sub>2</sub>O<sub>7</sub> [8].

In the temperature range  $700 - 800^{\circ}$ C CPP transforms into the  $\beta$ -Ca<sub>2</sub>P<sub>2</sub>O<sub>7</sub> modification, which is stable up to at least 1000°C. The density of monoclinic CPP is 2.936 g/cm<sup>3</sup>, and the density of the tetragonal modification is 3.128 g/cm<sup>3</sup> (Table 2). The structural rearrangement occurring on heating is accompanied by a 5.9% decrease of the volume. According to some data, on cooling this high-temperature phase of CPP can remain in the structure of materials containing HAP as a second phase [7].

A frit of the system  $CaO - P_2O_5$  (Ca : P = 0.20 – 0.75) can serve as a source of CPP; it is added as a sintering aid liquid-phase sintering followed by crystallization (US patent No. 437168). Ceramic can be made from CPP powder using Na<sub>4</sub>P<sub>2</sub>O<sub>7</sub> as a sintering aid [9]. According to the data provided in US patent No. 4861733, the  $\alpha$ -Ca<sub>2</sub>P<sub>2</sub>O<sub>7</sub> phase is formed at a high temperature after porous HAP is treated with solutions of H<sub>3</sub>PO<sub>4</sub> or (NH<sub>4</sub>)<sub>2</sub>HPO<sub>4</sub>. Materials containing a CPP phase can be obtained by mixing HAP-based powder systems with water and phosphoric or pyrophosphoric acid [7].

The objective of our work is to obtain composite ceramic materials containing CPP as a resorbable phase. We regulated the resorption limit by changing the mass content of the bioresistive phase in the initial batch from 0 to 100%. Monetite served as the source of the CPP phase. HAP and monetite were synthesized from solutions resulting from the interaction of calcium phosphate and ammonium hydrophosphate according to the following reactions:

TABLE	1
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Ca <sub>2</sub> P <sub>2</sub> O <sub>7</sub> -	Unit-cell parameters			Space	Coordi-	
	<i>a</i> , Å	$b, \mathrm{\AA}$	<i>c</i> , Å	β, deg	group	nation
β	6.684	6.684	24.144	90.0	P4 <sub>1</sub>	8
α	12.660	8.542	5.315	90.3	$P2_1/n$	4

TABLE 2	2
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C IN	СРР		
Card No.	modification	density, g/cm <sup>3</sup>	
73-440	Monoclinic	2.936	
9-345	Orthorhombic	2.950	
33-297	Tetragonal	3.128	
71-2123	"	3.129	
81-2257	"	3.127	
9-346	"	3.120	

the reaction proceeding at pH = 9 and 7 where calcium phosphate reacts with ammonium hydrophosphate was used to synthesize HAP [10]:

$$10Ca(NO_3)_2 + 6(NH_4)_2HPO_4 + 8NH_4OH = Ca_{10}(PO_4)_6(OH)_2 + 20NH_4NO_3 + 6H_2O;$$

the reaction proceeding at pH = 5 where calcium phosphate reacts with ammonium hydrophosphate was used to synthesize monetite [11]:

$$Ca(NO_3)_2 + (NH_4)_2HPO_4 + 2H_2O = CaHPO_4 \cdot 2H_2O \downarrow + 2NH_4NO.$$

The compositions of the mixtures used to obtain a composite ceramic with a bioresorbable phase are presented in Table 3. A uniform distribution of the components in the batch was obtained by mixing them in ball mill with the ra-

	Content, %		XPA phase composition	
Sample	HAP (Ca: P = 1.67, pH = 9)	monetite (Ca : $P = 1.00$ , pH = 5)	before heat-treatment	after heat-treat- ment at 1100°C
1	100	0	HAP, NH <sub>4</sub> NO <sub>3</sub>	HAP
2	80	20	HAP, monetite	НАР, β-ТСР
3	60	40	Same	ΗΑΡ, β-ΤCΡ, β-CPP
4	40	60	"	Same
5	20	80	"	β-TCP, β-CPP
6	0	100	Monetite, NH <sub>4</sub> NO <sub>3</sub>	β-СРР



**Fig. 2.** TG (*a*) and DTG (*b*) of HAP powder (sample 1), monetite powder (sample 6), and a mixture of HAP and monetite powders (sample 3).

tios balls : acetone : material = 3 : 1 : 1, after which the mixture was passed through a sieve with 200 µm cells.

XPA data (the temperature dependences of the mass loss and rate of mass loss were obtained using a Perkin Elmer (USA) Pyris thermal analyzer) show the initial powders after synthesis to be a mixture of calcium phosphate (HAP or monetite) and ammonium nitrate. A peak corresponding to the decomposition of ammonium nitrate is present near 200°C in the DTG curves (Fig. 2) for HAP and monetite. For monetite the mass losses in the temperature range 400 – 500°C correspond to the conversion of monetite into CPP.

The first three stages of the mass loss for a mixture of HAP and monetite (see Fig. 2) are a superposition of processes involving HAP and monetite, i.e., the loss of water ad-

sorbed in HAP and monetite and crystallization water in the supposed residual brushite. The next two stages are the decomposition of ammonium nitrate and the conversion of monetite into pyrophosphate. The conversion of monetite into calcium pyrophosphate in the presence of HAP was observed in the temperature range  $400 - 500^{\circ}$ C. Substantial mass losses were observed in the range  $600 - 1050^{\circ}$ C, which can be explained by the interaction of the phases present with the formation of TCP.

The data from dilatometric studies of the compacts (pressure 100 MPa) of the compositions 1, 3, and 6 are presented in Fig. 3 (the temperature dependences of the changes in the lineal samples were obtained using a NETSCH (German) dilatometer). The dilatometric curves for HAP and monetite



**Fig. 3.** Dilatometric curves for the following compositions: *1* ) 100% HAP (sample 1); *2* ) 100% monetite (sample 6); *3* ) mixture 60% HAP and 40% monetite (sample 3).

(CPP) are different from one another. The HAP curve is characterized by two steps. Melting and decomposition of ammonium nitrate occur near 250°C; densification starts above 600°C, i.e., in this temperature range the change of the lineal dimensions is due to the removal of pores and densification of the blank, which corresponds to sintering of HAP-based ceramic. For HAP the maximum shrinkage rate lies in the range  $850 - 950^{\circ}$ C. For monetite (CPP) two steps are observed below 1000°C on the curve of continual shrinkage: 450 - 550 and  $800 - 930^{\circ}$ C. The first interval corresponds to the conversion of monetite to CPP and second to densification onset during sintering of CPP.

The dilatometric curves of the compositions containing HAP and monetite (CPP) are a superposition of the curves for HAP and monetite. They have three steps, which are less distinct than those for the corresponding process in HAP or (and) monetite. The course of the curve for a mixture of monetite and HAP (and above 500°C for CPP and HAP) is similar to that of the dilatometric curve of monetite (CPP). Evidently, the plate morphology of monetite particles which CPP inherits impedes densification because of the sintering-active HAP.

The XPA data for samples 1, 3, and 6 calcined at different temperatures for 6 h are presented in Fig. 4. For the composition containing monetite and HAP before calcination, not only were the HAP and CPP phases observed but so was the TCP phase. The formation of TCP agrees with the data from thermal analysis (see Fig. 2). Indeed, according to the published data [2],  $\beta$ -Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub> ( $\beta$ -TCP, "true" calcium orthophosphate) is a high-temperature phase and can be obtained only during solid-phase synthesis. The interaction of calcium phosphates in the ratios Ca : P < 1 and Ca : P > 1, taken in the required amounts, is necessary for solid-phase synthesis of TCP (Ca : P = 1.5). In the present case CPP (Ca : P = 1.00) and HAP (Ca : P = 1.67) interact:

$$\operatorname{Ca}_{10}(\operatorname{PO}_4)_6(\operatorname{OH})_2 + \operatorname{Ca}_2\operatorname{P}_2\operatorname{O}_7 \to 4\operatorname{Ca}_3(\operatorname{PO}_4)_2 + \operatorname{H}_2\operatorname{O}^{\uparrow}.$$

Photomicrographs of samples of the ceramic calcined at 1100°C are presented in Fig. 5 (the photomicrographs of the



**Fig. 4.** XPA of samples 1 (*a*), 3 (*b*), and 6 (*c*): 1, 2, and 3) calcination temperature 900, 1000, 1100°C, respectively;  $\odot$ ) HAP; \*)  $\beta$ -Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub>;  $\triangle$ )  $\beta$ -Ca<sub>2</sub>P<sub>2</sub>O<sub>7</sub>.

ceramic were obtained using a LEO SUPRA-50VP Zeiss (Germany) scanning electron microscope). The microstructure of the ceramic with 100% HAP shows a substantial number of intercrystallite pores, which corresponds to the geometric density 88% (Table 4) and reflects an undersintered state of the material. Material with this composition sinters to a dense state (94%) during calcination at 1200°C for 6 h. Nonetheless, the materials with composition 1 after 6-h calcination exhibit the highest lineal shrinkage of all other compositions. It equals 13, 16, and 21% at 900, 1000, and 1100°C, respectively.

Ceramic with 100% CPP consists of quite large grains  $-20-30 \mu m$ . The microstructure of the ceramic with compo-



**Fig. 5.** Photomicrograph of samples 1 (*a*), 3 (*b*), and 6 (*c*) after calcination at 1100°C with a 6-h holding time.

sition 3 (HAP, TCP, and CPP) is different from that of the individual components. The photomicrographs show  $3 - 5 \mu m$ CPP grains, undersintered sections of HAP with particles less than 1  $\mu m$  in size, and TCP grains of the order of 1  $\mu m$  in size, which form along the periphery of the CPP grains. The arrangement and grain-size of the phases show that in such a system sintering, accompanied by a solid-phase reaction with the formation of TCP, retards the growth of CPP grains. It is reported in [11] that  $\beta$ -CCP in amounts 0.5 - 3.0 wt.% stabilizes the  $\beta$ -TCP phase at least up to 1200°C and can be used as an aid for calcination at higher temperatures than admissible for ceramic based on  $\beta$ -TCP.

The density of the composite ceramic after calcination at 900, 1000, and  $1100^{\circ}$ C is 1.49 - 2.10, 1.53 - 2.25, and 1.95 - 2.81 g/cm<sup>3</sup>, respectively. The density of samples 2 - 5 is lower than that of the HAP- or CPP-based materials (see Table 4).

The difference in the morphology of HAP and monetite particles obtained and the presence of substantial quantities

ТА	BL	Æ	4

Sample	Composition of the initial batch, % -	Relative density, %, at calcination temperature, °C		
		900	1000	1100
1	100 HAP	66.5	70.1	88.2
3	$60 \text{ HAP} + 40 \text{ monetite}^*$	53.1	55.9	71.3
6	100 monetite	59.9	77.1	80.1

\* The relative density of the HAP and monetite mixtures is approximate, since the materials based on them contain three phases whose quantities can be determined only approximately.

of ammonium nitrate make it difficult to obtain a high density of the ceramic containing several different phases. In addition, heating can activate other processes that affect the density of the sample — a modification transition of CPP, solid-phase reaction forming TCP, and so on.

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