EXCHANGE OF EXPERIENCE

RESORBABLE CALCIUM PHOSPHATES BASED CERAMICS

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Resorbable monophase ceramics and ceramic composites based on calcium pyrophosphate (CPP, $Ca_2P_2O_7$), tricalcium phosphate (TCP, $Ca_3(PO_4)_2$), and hydroxyapatite (HAp, $Ca_{10}(PO_4)_6(OH)_2$) were prepared via thermal treatment of a HAp (Ca/P = 1.67) and CPP (Ca/P=1) mixture. High-temperature solid-state reaction between HAp and CPP leading to TCP formation was studied within the range 700–800 °C. The metastable α -TCP phase was observed in this range as a product of the solid-state reaction. The reaction had been completed before sintering of the powders started. The microstructure of CPP/TCP composites was found to be duplex-like, consisting of large CPP grains with smaller TCP grains among CPP ones. In the case of the monophase ceramics with starting HAp/CPP ratio corresponding to TCP, grain size was less than 300 nm.

Keywords: resorbable monophase ceramics, ceramic composites, calcium pyrophosphate, tricalcium phosphate, hydroxyapatite, high-temperature solid-state reaction, microstructure.

INTRODUCTION

The regeneration approach for bone tissue repairing assumes application of new bioresorbable materials based on calcium phosphates. Resorbable (i.e., soluble in the organism liquids) materials exhibit osteostimulatory properties and, thus, increase the rate of replacement of an implant by native bone tissue. Traditional bulk materials based on hydroxyapatite (HAp, $Ca_{10}(PO_4)_6(OH)_2$) do not seem to be suitable for tissue repairing due to low resorption rate of the material (corresponding solubility product $K_s = 10^{-117.2}$ M¹⁸ [1]), as well as to poor osteoconducting and osteoinducting properties. A way to overcome the problem lies in preparing multiphase materials with resorbable phases, for instance, tricalcium phosphate (TCP, $Ca_3(PO_4)_2$ [2]), calcium pyrophosphate (CPP, $Ca_2P_2O_7$) [3, 4], bioglasses [5]. The mostly studied materials between the mentioned above are biphase composites HAp/TCP [6, 7]. At the same time, ceramic materials containing CPP as a resorbable component are not widespread. Perhaps, this is due to the formation of CPP crystalline hydrate causing calcium pyrophosphate deposition disease (CPDD). However, pyro- and polyphosphate ions play an essential role in biological processes of healthy organisms, including control of bone mineralization, while the cause of CPDD might be an immanent shift in bone metabolism for a diseased man. Reasoning from this, it is naturally to revisit ceramic materials made of CPP and to develop preparation routes for CPP ceramics or ceramic composites.

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Variation the ratio resistive phase (HAp)/resorbable phase (CPP or TCP) ratio unequivocally allows regulating the rate of biomaterial resorption in a wide range suitable for a certain clinical case. Taking into account the high-temperature reaction between HAp and CPP with TCP formation (reaction (1)), this ratio can be varied by changing the composition of starting mixture and conditions of thermal treatment:

$$Ca_{10}(PO_4)_6(OH)_2 + Ca_2P_2O_7 = 4Ca_3(PO_4)_2 + H_2O.$$
 (1)

Features of the reaction between HAp and CPP and their effect on microstructure of the composites were the aim of the present work.

EXPERIMENTAL

Preparation of Brushite, CPP, and HAp Powders. Hydroxyapatite was synthesized via wet precipitation technique from stock $Ca(NO_3)_2$ and $(NH_4)_2HPO_4$ solutions:

$$10Ca(NO_3)_2 + 6(NH_4)_2HPO_4 + 8NH_4OH \rightarrow Ca_{10}(PO_4)_6(OH)_2 \downarrow + 20NH_4NO_3 + 6H_2O$$
(2)

at $[Ca^{2+}] = 1.3$ M, $[HPO_4^{2-}] = 1$ M, $T = 60^{\circ}$ C, pH = 9.0 ± 0.3. The precipitate was filtered and dried for 48 h in air. To decompose the by-product of the reaction (ammonium nitrate), the powders were annealed at 300°C for 3 h.

Brushite (CaHPO₄ · 2H₂O) was obtained by quick mixing of the stock solutions without pH regulation [8] according to reaction (3). The pH level during interaction was in the range 4.5-5.0:

$$Ca(NO_3)_2 + (NH_4)_2HPO_4 + 2H_2O \rightarrow CaHPO_4 \cdot 2H_2O \downarrow + 2NH_4NO_3$$
(3)

at $[Ca^{2+}] = 0.5 \text{ M}, [HPO_4^{2-}] = 0.5 \text{ M}.$

Calcium pyrophosphate was prepared by brushite decomposition at 600°C (3 h), according to the reaction:

$$2CaHPO_4 \cdot 2H_2O = Ca_2P_2O_7 + 5H_2O.$$
 (4)

Starting mixtures to fabricate composite materials (Table 1) were made from HAp and CPP powders by mixing in a planetary-ball mill and subsequent pressing of the powders under 100 MPa.

To study phase transformations in the mixtures, the samples made from powder mixture #3 were annealed at different temperatures in the range 700–800°C for 2 h (rate of heating to a certain temperature was 5°C/min). The compacts of all powders (#1 and #4) and powder mixtures (#2 and #3) were annealed at 900, 1000, and 1100°C with isothermal holding up to 6 h (heating rate to these temperatures was 5°C/min) to obtain monophase ceramics and ceramic composites.

To investigate the mechanism of solid-state reaction between HAp and CPP, two sintered pellets of HAp (density 92%) and β -CPP (density 80%) were prepared, polished, pressed to each other (with a shift of one pellet with respect to another one in order to make a natural mark of initial interface), and annealed at 1100°C for 48 h under constant loading of ca. 1 N (Fig. 1). After that, this diffusion pair was cut across the layer of the reaction product, and microstructure of this layer was inspected by SEM. Relative volume changes during phase transformations were calculated using crystallographic densities of HAp (3.16 g/cm³), α -TCP (2.831 g/cm³), β -TCP (3.07 g/cm³), CaO (3.35 g/cm³), α -CPP (2.95 g/cm³), and β -CPP (3.13 g/cm³) borrowed from the ICSD PDF-2 database. Density of the sintered pellets was estimated from geometrical measuring the volume and weighing a pellet.

Sample notation	HAp/CPP ratio in starting powder mixture (wt.%)	Phase composition of the material (wt.%) after completing reaction (1)
#1 (HAp)	HAp (100)	HAp (100)
#2 (TCP)	HAp (80) / CPP (20)	TCP (100)
#3 (TCP/CPP)	HAp (40) / CPP (60)	TCP (50) / CPP (50)
#4 (CPP)	CPP (100)	CPP (100)

TABLE 1. Samples under Study



between HAp and CPP

Characterization of Samples. X-ray diffraction (XRD) patterns were obtained with $Cu-K_{\alpha}$ -radiation using Rigaku D/Max-2500 with a rotating anode (Japan). Phase composition was estimated by the Chung method [9]. Microstructure of the powders and dense specimens was observed by SEM at 5–10 kV (FESEM LEO Supra 50 VP, Carl Zeiss, Germany). To reveal the microstructure, the samples were polished with diamond pastes (down to 1 µm) and silica suspension (OP-S with a grain size less than 1 µm, Struers, Denmark), and then thermally etched at 900–1000°C for 30 min. Composition of the samples (Ca/P ratio) was determined by SEM/EDX (INCA Energy+, Oxford Instruments, UK). Linear shrinkage of the samples was studied using a DI 24 dilatometer (ADAMEL LHOMARGY, France), heating rate was 5°C/min.

RESULTS AND DISCUSSION

Phase Transformations in CPP. According to the CaO–P₂O₅ phase diagram [5], β -Ca₂P₂O₇ and α -Ca₂P₂O₇ phases are thermodynamically stable and γ -Ca₂P₂O₇ is a metastable phase. There is some information on the range of γ -phase formation, but very little is known about properties of the γ -phase, e.g., its crystal structure. However, it is apparent that high-temperature polymorphism in CPP (and phase transition between polymorphs) greatly influences kinetics of HAp and CPP interaction. The γ -to- β phase transition was investigated using quantitative XRD. The phase transition begins at temperature of about 700°C, but significant content of β -phase was found at temperature of about 770°C.

Study of Phase Transformations in the Powder Mixtures. Figure 2 shows the weight fraction of the phases vs. temperature for sample #3(TCP/CPP) annealed at different temperatures in the range 700–800°C for 2 h. As a



Fig. 2. Weight fraction of the phases vs. temperature for sample #3 (TCP/ CPP)

result of reaction (1) between HAp and CPP, a metastable high-temperature phase of calcium orthophosphate (α -TCP) was observed. The fact of α -TCP formation at relatively low temperature in the course of thermal evolution of amorphous tricalcium phosphate was reported earlier [10]. The reason for it is structural similarity between α -TCP and HAp (there are areas in crystal structure of the high-temperature TCP phase resembling that in the structure of HAp [11]). A further increase in temperature decreases the fraction of the α -phase, and this is related to α -TCP $\rightarrow \beta$ -TCP conversion, starting at 760°C. For the samples annealed at the temperature in the range 900–1100°C, only β -phase formation is observed. Samples #2 and #3(TCP/CPP) show similar behavior with a glance of γ -CPP into β -CPP phase transformation.

Thus, using these curves of phase fraction vs. temperature, it is possible, in principle, to obtain composite materials with a preset phase ratio and, consequently, with preset resorption properties (e.g., rate of resorption). Let us stress here that there is a possibility to prepare both bi-phase composites HAp/ α -TCP and three-phase composites HAp/ α -TCP/ β -TCP within the proposed route.

Study of the Reaction Mechanism. SEM analysis of the diffusion zone in contacting pellets of HAp and β -CPP revealed fine-grained TCP extending from the initial boundary between HAp and CPP towards the bulk of HAp pellet (Fig. 1, 3). The reactions below reflect the processes taking part on HAp/TCP and TCP/CPP boundaries, respectively:

$$Ca_{10}(PO_4)_6(OH)_2 \rightarrow 3\alpha - Ca_3(PO_4)_2 + CaO + H_2O, \Delta V/V = +8.2\%,$$
 (5)

$$\beta - \operatorname{Ca}_2 \operatorname{P}_2 \operatorname{O}_7 + \operatorname{CaO} \to \alpha - \operatorname{Ca}_3(\operatorname{PO}_4)_2, \Delta V/V = +3.5\%.$$
(6)

The essence of reaction (4) consists, thus, in a transfer of calcium and oxygen ions from the HAp area (this is a source of calcium and oxygen, as shown by reaction (5)) into the CPP area (a sink of Ca and O, reaction (6)). First, α -TCP is formed and relative volume of the system is increased by 8% (without consideration of water vapor release), and then the α -phase is transformed into the β -phase accompanied by volume decreasing:

$$\alpha - \operatorname{Ca}_3(\operatorname{PO}_4)_2 \to \beta - \operatorname{Ca}_3(\operatorname{PO}_4)_2, \Delta V/V = -7.8\%.$$
⁽⁷⁾

However, in the CPP area, the volume effect of reaction (6) is noticeably positive and corresponds to volume increase by 3.5%. Volume changes in the material are the cause of significant mechanical stresses. The stresses lead to crush of large grains and prevention of grain growth, and, therefore, fine-grained TCP areas are formed. Note that water vapor elimination also facilitates cracking of the particles and, thus, enhances the flux of calcium and oxygen ions via surface diffusion.

Study of Densification of the Composites. The study of densification reveals different temperature ranges for solid-state reaction and sintering. XRD patterns allow concluding that the solid-state reaction is developed in the temperature range about 700–800°C and is fully completed by 900°C. Meanwhile, sintering begins at the temperature 900°C. Sample #4 (CPP), annealed at 1100°C for 6 h, shows the maximal density among the samples



Fig. 3. Microstructure of the HAp/CPP diffusion zone after 1100°C, 48 h



Fig. 4. Density of the composites vs. temperature of annealing (isothermal conditions) (*a*), linear shrinkage curve (heating rate 5° C/min) (*b*)

based on powder mixtures containing CPP (Fig. 4*a*). The pronounced density decreasing for the samples annealed at the temperature of about 1200°C is related to the β -CPP $\rightarrow \alpha$ -CPP and β -TCP $\rightarrow \alpha$ -TCP transformations accompanied by the significant volume decreasing (see reactions (7) and (8)):

$$\alpha - \operatorname{Ca}_2 P_2 O_7 \to \beta - \operatorname{Ca}_2 P_2 O_7, \, \Delta V/V = -6.1\%.$$
(8)

Note that the sintering process is divided into three stages. Linear shrinkage in the temperature range 700–800°C can be attributed to reaction (1), the stage in the temperature range 900–1000°C concerns CPP and TCP sintering, and the phase transformation in the temperature range about 1050–1100°C is observed (Fig. 4*b*). In a series of samples $\#2(\text{TCP}) \rightarrow \#3(\text{CPP/TCP}) \rightarrow \#4(\text{CPP})$ (CPP content increasing), densification rate increase in the temperature range 900–1000°C is evidenced.

Microstructure of the Samples under Study. Figure 5*a* shows bimodal grain size distribution for sample #3(CPP/TCP). Relatively coarse grains correspond to the TCP-phase and fine-grain areas correspond to the CPP-phase, as it was confirmed by EDX analysis of the areas. Surprisingly, sample #2(TCP) demonstrates fine-grain microstructure with a grain size of about 200–300 nm (Fig. 5*b*). To our mind, the solid-state reaction of TCP synthesis is a reason for fine-grained microstructure. It was considered earlier that mechanical stresses arising from volume changes in the course of the reaction could be the cause of retardation of TCP grain growth. This is true for the case of sample #2 where complete run of reaction (1) leads to a mono-phase specimen. However, for the case of biphase sample #3 demonstrating a higher rate of grain boundary movement (for TCP grains), additional factors having stimulatory effect on recrystallization of TCP are to be assumed. Bearing in mind that the rate of boundary movement (v_b) is a product of boundary mobility (M_b) and driving force for boundary movement (F_b): $v_b = M_b \cdot F_b$, one has to consider both contributions:

(i) M_b (which is proportional to the coefficient of bulk diffusion D) increases due to lowering activation energy of diffusion in the presence of CPP phase. It is possible, in principle, accounting for certain nonstoichiometry of



Fig. 5. Microstructure of samples #3(TCP/CPP) (a) and #2(TCP) (b), 1100°C, 6 h

the TCP phase. Then, the composition of TCP in the TCP+CPP biphase mixture (invariant from the viewpoint of the CaO-P₂O₅ phase diagram) stands for a low-Ca boundary of the TCP homogeneity area, i.e., for the composition with Ca-vacancies. There are few evidences for that, e.g., a noticeable shift of the temperature of phase transition $\beta \rightarrow \alpha$ for TCP in the presence of CPP [12], aliovalent substitution of Ca with alkaline metals M up to composition Ca_{2.86}M_{0.29}(PO₄)₂ at least [13]. The β -TCP phase is quite close to glaserite-like phases demonstrating rather broad areas of solid solutions due to shifts of cations from ideal positions, rotation of PO₄-tetrahedra, and cation disordering between nonequivalent positions in the lattice [14]. Such facts argue for noticeable transport of cations and, perhaps, holes.

(ii) F_b can be originated not only from grain boundary curvature, but additional chemical impact on recrystallization due to difference of actual chemical potential of CaO in TCP areas and an equilibrium potential at a given temperature (which is, in fact, constant for invariant mixture TCP + CPP and is defined at TCP/CPP interface) can take place. It is usually accepted that the chemical driving force exceeds the one predetermined by grain boundary curvature, at least, in an order of magnitude (see, e.g. [15, 16]). However, this chemical driving force can become effective only if structural reasons for the diffusion flux of Ca and O atoms exist. Such a note implies, again, nonstoichiometry of the TCP phase.

To our best knowledge, the issue of point defects in TCP (and related non-stoichiometry phenomenon) was not treated in the available literature, and it was not the subject of the present work either. At the same time, in view of the above data, the work on defect structure of TCP is awaited.

CONCLUSIONS

In the temperature range 700–800°C, the solid-state reaction between HAp and CPP leading to the formation of TCP takes place. Varying thermal treatment conditions (temperature and duration of treatment) allow obtaining a composite with preset phase composition and adjusted resorptivity.

Microstructural study of the samples reveals the formation of fine-grained TCP as the solid-state reaction product. The route described in the paper gives an opportunity to fabricate ultrafine-grained phosphate ceramics with a grain size of about 300 nm. It is thought that such a ceramic material has enhanced resorption properties due to a highlarge ratio of grain boundary surface/volume.

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