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Calcium phosphate powders synthesized from calcium chloride and potassium hydrophosphate

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Abstract Porous ceramics based on $Ca_3(PO_4)_2$ (TCP) was obtained by sintering of a mixture of hydroxyapatite (HAp) and brushite ($CaHPO_4 \cdot 2H_2O$) powders. The main interaction of HAp + CPP ($Ca_2P_2O_7$) → TCP type in the composite sample HAp/brushite takes place at temperatures higher than 700 °C and leads to rather uniform porous microstructure. We have suggested that CPP-like phases (and especially $K_2CaP_2O_7$) undergo partial decomposition accompanied by evaporation of P_2O_5. The role of KCl—the by-product of solution synthesis of HAp and brushite powder precursors, consists in (i) it replace in part Ca in CPP phase making last one more reactive, (ii) it switches sintering of the ceramics in liquid-phase regime, (iii) at higher temperature it evaporates and, thus, contributes to formation of pores in the ceramics.

Keywords Calcium-phosphate biomaterials · Composites · Phase transformations · Calcium pyrophosphate · Hydroxyapatite · Tricalcium phosphate

Introduction

Fabrication of biomaterials for medical applications (e.g., for the use as bone implants), being a sufficient part of activity aimed at increasing quality of human life, demands radical steps and new findings in this area. The number of patients, required bone tissue substitution or treatment and variety of circumstances leading to it, grows enormously, while the choice of materials suitable for this aim is still scarce. The reason for it lies in that elaboration of modern biomaterials should take into account their biocompatibility and bioactivity causing rather special criteria of materials selection, viz. the requirement of chemical composition close to a bone one. Hence, long-term interest in calcium phosphates is explainable since they are main constituents of inorganic part of man's bone. Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HAp) is the most similar to the bone tissue in its chemical composition. It is also the calcium phosphate among others which has been repeatedly tested in medicine in forms of porous and compact materials. The main disadvantage of HAp is its low resorption rate (i.e. solubility in vivo), too sluggish to induce a massive formation of new bone tissue. Two ways to overcome this obstacle are suggested: (i) chemical modification of HAp to enhance its solubility, and (ii) fabrication of composite materials where pre-determined ratio of bioresistive (HAp) and bioresorbable (typically, $Ca_3(PO_4)_2$, or TCP) phases defines solubility of the material in organism [1]. TCP has three polymorphs, such as β-TCP stable below 1180 °C, α-TCP between 1180 °C and 1400 °C, and α'-TCP above 1470 °C. Among the three allotropic forms, β-TCP is preferred as a bioceramic on account of its chemical stability, mechanical strength and proper bioresorption rate [2].

In the frame of the second approach, phosphate phases other than β-TCP are under search now. One of possible candidates for this role is calcium pyrophosphate ($Ca_2P_2O_7$, CPP), its biocompatibility was proved in numerous experiments; in addition, it was demonstrated that CPP possesses osteostimulating and bioresorptive properties [3]. Thus, composites containing CPP are thought to be promise materials with enhanced level of bioresorption. X-ray diffraction studies of $Ca_2P_2O_7$ show that it exists in three

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different forms depending on the temperature of firing: γ-CPP below 750 °C, β-CPP between 750 and 1171 °C and α-CPP above 1171 °C [4].

It is worth noting that TCP has a rather long history of application. The main problem in fabrication of TCP ceramics comes from weak sinterability inherent to TCP itself. At the same time, one can prepare TCP in situ from CPP and HAp during heat treatment according to the following reaction:

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

Such a technique allows partially to solve the problem of sintering outlined above, as well as to adjust resorption rate of the composite by shifting HAp:CPP = 1:1 composition toward to HAp (and to make it more bioresistive) or, in opposite direction, toward to CPP (assuming better resorption). In principal, a priori variation of HAp/CPP ratio will permit to achieve biological properties of the composite suitable for a separate clinical case.

In this work we report on fabrication of biocompatible porous material based on TCP derived from HAp/CPP mixture in the course of its sintering. Porosity is provided by phase formation processes accompanied by release of a gaseous product. Thereby, phase transformations in the material under thermal treatment is of great importance; we have examined them by thermal analysis coupled with XRD analyses of quenched specimens.

In addition, we have studied the effect of the by-product (KCl in our case) of solution synthesis of precursors, including its chemical reactions with the calcium phosphates leading to formation of new phases, and its influence in densification and grain growth. The issue of by-products as components which do exert significant effect on phase and microstructure evolution of ceramics was considered in some works. For instance, the effect of by-products on HAp ceramics obtained in various conditions and from different precursors can be found elsewhere [5–11]. Application of salts as sintering additives is interesting and worth for examination. Essential number of salts has already been examined as sintering additives ex situ [12, 13]. This way of introduction of the additive suffers from possible inhomogeneity of additive distribution over the sample. The same salt in the form of a by-product seems to be distributed more uniform and, thus, leads to more uniform microstructure of the ceramics.

Experimental

Powder samples under study (brushite—$CaHPO_4{\cdot}2H_2O$, HAp and their mixture in ratio 1:1 calculated in account of CPP) and concentration of stock solutions of K_2HPO_4 and $CaCl_2$ are listed in Table 1. Calcium chloride and potassium hydrophosphate used to prepare the stocks solutions were of chemical grade purity.

Table 1 K_2HPO_4 and $CaCl_2$ solutions used to obtain calcium phosphate powders

Powder	C/K_2HPO_4/mol/l	C/$CaCl_2$/mol/l
Brushite	0.5	0.5
HAp	0.5	0.3
Brushite–HAp mixture	0.5 brushite/0.5 HAp	0.5 brushite/0.3 HAp

HAp was precipitated according to the reaction (2):

$$\begin{aligned}&10CaCl_2 + 6K_2HPO_4 + 8KOH\\&\quad = Ca_{10}(PO_4)_6(OH)_2\downarrow + 20KCl + 6H_2O,\end{aligned} \quad (2)$$

by dropwise addition of the potassium hydrophosphate solution with threefold amount of KOH to the calcium chloride solution at pH 9–10 and 60 °C under continuous stirring followed by maturation of the precipitate during 30 min in mother liquor. The precipitate was then filtered without washing.

Brushite precursor was precipitated according to the reaction (3):

$$CaCl_2 + K_2HPO_4 + 2H_2O = CaHPO_4 \cdot 2H_2O\downarrow + 2KCl, \quad (3)$$

by rapid pouring of the $CaCl_2$ solution into the K_2HPO_4 solution at 20 °C under vigorous stirring. The precipitate was then filtered without washing.

Resulted powders were allowed to dry in air overnight. Dry powders were disaggregated in a ball mill in acetone media with powder:acetone:balls ratio set to 1:1:5. The powders processed in this way were sieved (Saatilene HiTech^{TM} polyester fabrics, cells of 200 μm). The powders were uniaxially compacted into rectangular bars 10 × 5 × 2.5 mm in a stainless steel die under 100 MPa. The compacts were sintered for 6 h at the muffle furnace at various temperatures from 500 to 1100 °C and then cooled at furnace.

Densities of the green compacts and sintered samples were determined by geometrical measurements. Phase composition of powder precursors and compacted samples was examined by X-ray diffraction (XRD) in the interval of angles $2\Theta = 3$–$60°$ (Cu Kα radiation, Rigaku D/MAX 2500 with rotating anode, Japan). TGA/DTA of the specimens was conducted with a Diamond Pyris apparatus (Perkin Elmer, USA) in air up to 1000 °C at a heating rate of 10 °C/min. The linear shrinkage (by means of thermodilatometry, TD) of the compacts was determined with a NETZSH 402 dilatometer (NETZSCH, Germany) at a ramp rate of 10 °C/min and a LIR-1400 dilatometer (Russia) at a ramp rate of 5 °C/min. For these measurements, the bar-shaped samples of 6 × 4 × 10 mm were heated in air up to 900 °C. The microstructure of the powders and dense specimens was elucidated using

FESEM with a LEO Supra 50 VP scanning electron microscope (Carl Zeiss, Germany) operated at 5–10 kV.

Results and discussion

Brushite and HAp

According to XRD analysis (Figs. 1, 2), the powders contained only corresponding main phase (brushite or HAp) and by-product (KCl).

The HAp powder was composed of equiaxed particles of 100–200 nm, while particles of the brushite powder demonstrated plate-like habits with dimensions of plates of 15–20 µm, as it was evidenced by FESEM. Specific morphology of the brushite powder is reflected in free density of the powder 0.28 g/cm^3 being less compared to 0.4 g/cm^3 for the HAp one. However, this difference was eliminated for green density of the compacts, being 1.5 g/cm^3 and 1.4 g/cm^3 for brushite and HAp, respectively.

According to thermoanalitical curves (TG in Fig. 3, and linear shrinkage curve TD in Fig. 4), it is apparent that distinct changes in the samples occur at ca. 200, 400, 600 and 800 °C. Prominent mass loss and contraction of the samples of brushite and HAp/brushite mixture are connected with known process of removal of crystalline water from brushite lattice and formation of monetite (anhydrous $CaHPO_4$) in accordance with the reaction [14]:

$$CaHPO_4 \cdot 2H_2O = CaHPO_4 + 2H_2O\uparrow . \quad (4)$$

Mass loss (and corresponding sample contraction) in the region of 400–600 °C is usually attributed to conversion of hydrophosphate anion into pyrophosphate one [14]:

$$2CaHPO_4 = Ca_2P_2O_7 + H_2O\uparrow . \quad (5)$$

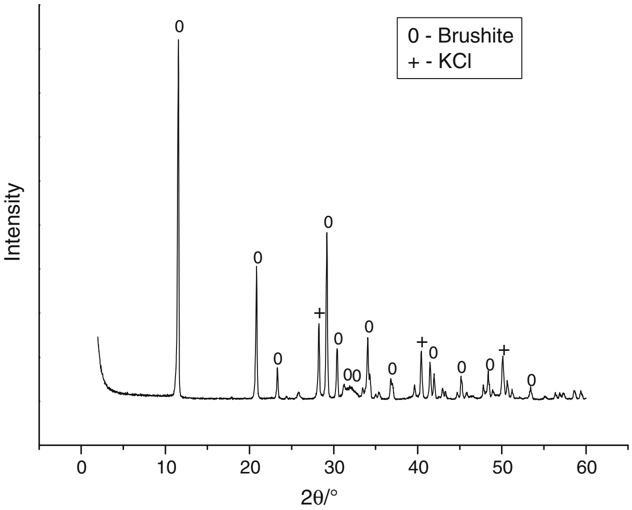

Fig. 1 XRD of the as-precipitated brushite powder

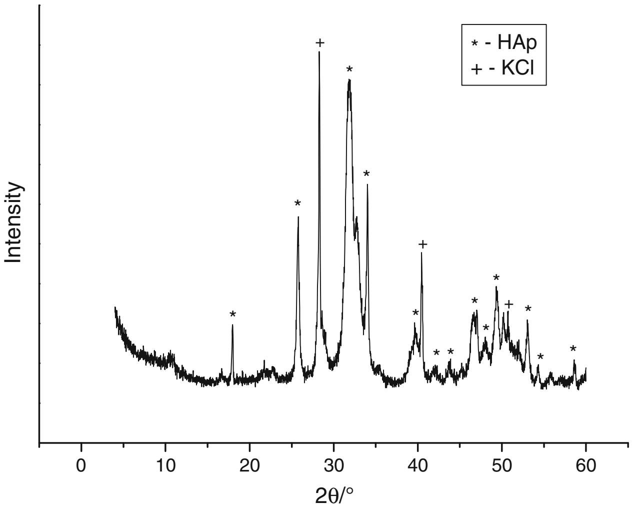

Fig. 2 XRD of the as-precipitated HAp powder

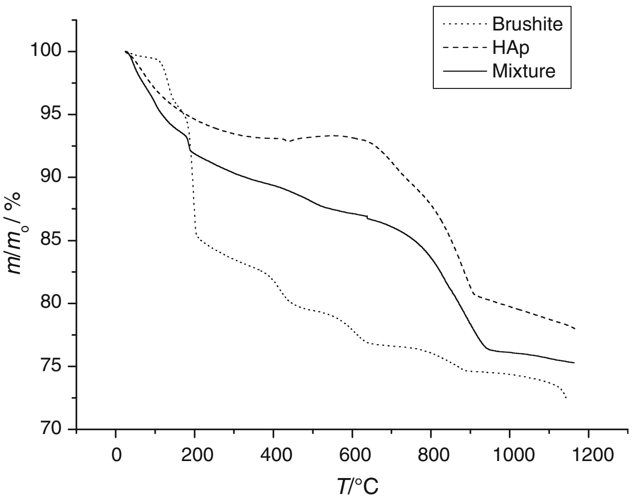

Fig. 3 TG curves of brushite, HAp and their mixture

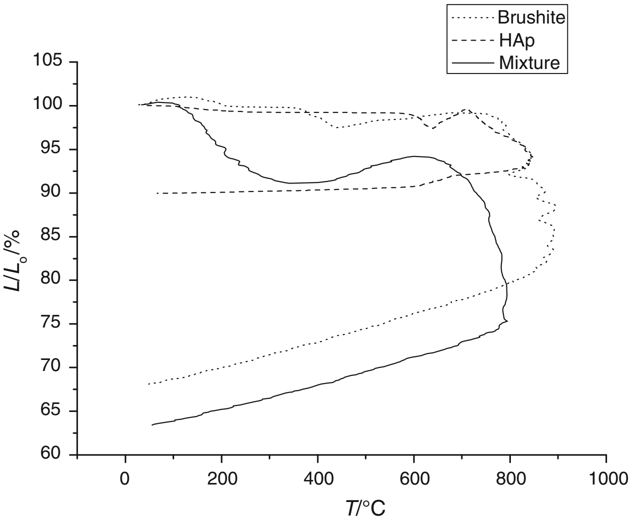

Fig. 4 Shrinkage curves (TD) of brushite, HAp and their mixture

Table 2 Phase composition of samples annealed upon various temperatures

Temperature/°C	Brushite	HAp	Brushite/HAp mixture
500	β-$Ca_2P_2O_7$, $K_2CaP_2O_7$, $Ca_5(PO_4)_3Cl$, KCl	HAp, KCl	β-$Ca_2P_2O_7$, $K_2CaP_2O_7$, $Ca_5(PO_4)_3Cl$, HAp, KCl
600			
700	$K_2CaP_2O_7$, $Ca_5(PO_4)_3Cl$		β-$Ca_3(PO_4)_2$, ($Ca_{10}K(PO_4)_7$), HAp, KCl
800	$K_2CaP_2O_7$, β-$Ca_3(PO_4)_2$, $Ca_{10}K(PO_4)_7$	HAp	β-$Ca_3(PO_4)_2$, ($Ca_{10}K(PO_4)_7$), HAp
900		HAp, CaO	β-$Ca_3(PO_4)_2$, ($Ca_{10}K(PO_4)_7$)
1000			
1100			

It is of note that in pure brushite, the reaction (5) is completed to 600 °C and TG curve usually demonstrates a plateau of constant mass, whereas in the presence of the by-product in our case, mass loss steps are situated even at higher temperatures. We have to conclude the presence of the by-product drastically changes kinetics of the reaction (5) due to formation of other than CPP products (for details, see Table 2). Nevertheless, the processes occurring in brushite samples in the range 200–400 °C are well-documented, so they will be out of the scope of our detailed discussion.

The origin of events detected by TG and TD can be deduced from analysis of phase composition of the annealed samples (Table 2).

Apparently, below 700 °C an interaction of monetite and KCl is not completed, as $Ca_2P_2O_7$ and KCl are still observed in XRD spectra. The main result of this interaction is formation of potassium-doped CPP, $K_2CaP_2O_7$ (chlorapatite, $Ca_5(PO_4)_3Cl$, is an admixture). Interestingly, that in the case of interaction of CPP with NaCl, the major product is sodium-doped orthophosphate $NaCaPO_4$ with β-rhenanite structure [P. Evdokimov, Private communication]. The phase of tricalcium phosphate (which contains an admixture of potassium-substituted $Ca_{10}K(PO_4)_7$ with β-TCP structure either) is formally generated from potassium-calcium pyrophosphate and chlorapatite, existing in the sample in ratio ca. 2:1. However, corresponding reaction cannot be balanced since the ratio Ca/P in its left part (i.e. for the mixture of $K_2CaP_2O_7$ and $Ca_5(PO_4)_3Cl$ stoichiometrically equivalent to the parent phase of monetite, and having, therefore $Ca/P = 1$) is noticeable less than that one in the right part (i.e. for the mixture of $Ca_3(PO_4)_2$, $Ca_{10}K(PO_4)_7$, where $Ca/P \to 1.5$) of the hypothetical equation. Thus, we have to postulate formation of another phase with $Ca/P < 1$ (see Eq. 8[1]).

Appearance of the CaO phase at the HAp-based sample argues that as-precipitated powder does contain carbonate-substituted HAp $Ca_{10}(PO_4)_{6-2x}(CO_3)_{3x}(OH)_2$, which is XRD similar to stochiometric HAp. Then, at 800–900 °C a decomposition of carbonated HAp takes place:

$$\begin{aligned} &Ca_{10}(PO_4)_{6-2x}(CO_3)_{3x}(OH)_2 \\ &\quad = (1 - 1/3x)Ca_{10}(PO_4)_6(OH)_2 \\ &\qquad + 10x/3CaO + 3xCO_2\uparrow + x/3H_2O\uparrow . \end{aligned} \tag{6}$$

It is essential that not all reactions occurred in the samples run in pure solid-state regime. Potassium chloride has a melting point at 771 °C. The TD curve for the HAp sample demonstrates a feature around 800 °C, afterward, mass loss and densification (detected as sample contraction) for all types of the samples increase significantly (Figs. 3, 4). Although boiling point of KCl is situated at ca. 1400 °C, its evaporation evidenced by mass-loss trend at the TG curves at temperatures higher than 1000 °C (KCl can be visualized in deposits from vapour phase onto cold parts of a furnace) does take place.

From the view-point of the processes described above, it is interesting to discuss data on densification of corresponding ceramics. Density of the sintered samples versus temperature is shown in Fig. 4. Density of samples based on brushite and HAp passes through several stages:

(1) 500–700 °C. Density of samples based on brushite decreases owing to mass loss superposed with the absence of sintering, while HAp density increases, which is explained by mass constancy and rising sintering intensity.

(2) 700–1000 °C. Density of brushite-based samples rises and reaches its maximum at 1000 °C. In the case of HAp, we observe superposition of phase formation and intensification of sintering process.

(3) 1000–1100 °C. KCl release becomes possible at that temperature range, leading to decrease of brushite-based samples. In the case of HAp, decrease of density can be attributed to subsequent evaporation of KCl and coalescence of emerging pores; these two processes look as deceleration of densification of the sample and even as its swelling.

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[1] Note that vitreous potassium polyphosphate phase $(KPO_3)_n$ cannot be detected by XRD, its presence was postulated by us from the view-point of stoichiometry and feasible phase relations in $CaO–K_2O–P_2O_5$ system.

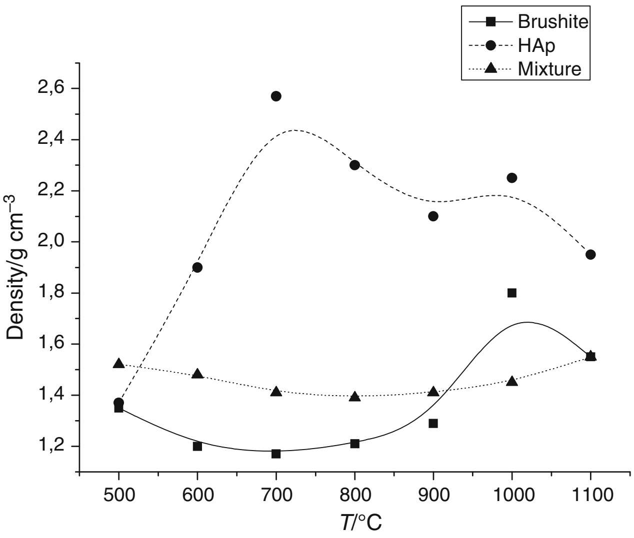

Fig. 5 Density of the sintered samples based on brushite, HAp and their mixture

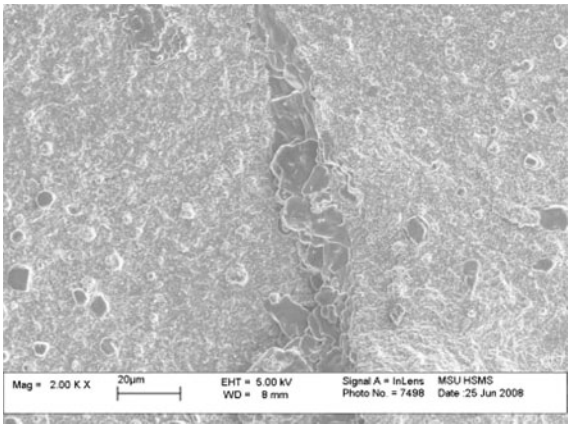

Fig. 6 HAp-based ceramics sintered at 700 °C

According to SEM data (Fig. 5), at temperature of 700 °C and less one can observe a picture of sintering essentially in solid-state regime. Crystals of KCl (black plygons) are situated chaotically over the HAp sample. The sample looks rather dense.

At higher temperatures (Fig. 6), sintering runs mainly by liquid-phase mechanism. Ceramics is porous due to anisotropic grain growth and release of KCl.

Brushite–HAp mixture

Based on previously mentioned data on phase composition and thermal analysis of the samples we can now construct the full sequence of phase transformations in the ceramics under study in the interval 500–1100 °C:

$$\begin{aligned}&7Ca_2P_2O_7 + 8KCl + 3H_2O\\&\quad = 4K_2CaP_2O_7 + 2Ca_5(PO_4)_3Cl + 6HCl\uparrow\\&\{Ca_2P_2O_7 + 2KCl = K_2CaP_2O_7 + CaCl_2\\&2Ca_2P_2O_7 + 2KCl + H_2O\\&\quad = Ca_3(PO_4)_2 + K_2CaP_2O_7 + 2HCl\uparrow\\&3Ca_3(PO_4)_2 + CaCl_2\\&\quad = 2Ca_5(PO_4)_3Cl\}\quad 500-700\,^{\circ}C\end{aligned}\tag{7}$$

$$\begin{aligned}&2K_2CaP_2O_7 + 2Ca_5(PO_4)_3Cl\\&\quad = 4Ca_3(PO_4)_2 + 2KCl\uparrow + 2/n(KPO_3)_n\\&(2K_2CaP_2O_7 + 4Ca_5(PO_4)_3Cl\\&\quad = 2Ca_{10}K(PO_4)_7 + 2/n(KPO_3)_n\\&\qquad + 2CaCl_2\uparrow)\quad 700-800\,^{\circ}C\end{aligned}\tag{8}$$

$$\begin{aligned}&Ca_{10}(PO_4)_{6-2x}(CO_3)_{3x}(OH)_2\\&\quad = (1-1/3x)Ca_{10}(PO_4)_6(OH)_2 + 10x/3CaO\\&\qquad + 3xCO_2\uparrow + x/3H_2O\uparrow\quad 800-900\,^{\circ}C\end{aligned}\tag{9}$$

$$\begin{aligned}&2Ca_{10}(PO_4)_6(OH)_2 + K_2CaP_2O_7\\&\quad = 7Ca_3(PO_4)_2 + H_2O\uparrow + 2KOH\end{aligned}\tag{10}$$

It should be stressed that in the case of the brushite/HAp mixture, the picture of phase transformations is not just a simple superposition of the transformations in the constituents since the interaction between HAp (and/or chlorapatite) and CPP (and/or $K_2CaP_2O_7$) (see the reactions (8), (10)) takes place. of each other properties by reason of above-state interaction. This interaction is supposed to affect key characteristics of the material—its phase composition, biodegradability, bioactivity, porosity, mechanical properties. It is possible now to describe the changes in density of the ceramics based on the brushite/HAp mixture (see corresponding curve in Fig. 4):

(1) 500–800 °C. Decreasing of density is associated with mass loss of the sample (as it is evidenced by TG data). Sintering has not occurred yet, therefore, particles does not approach each other and linear dimensions do not practically change.
(2) 800–1100 °C. One can observe an increase of density of the sample. This tendency can be explained by intensive liquid-phase sintering, and in spite of prominent mass loss of water, CO_2 and the release of the by-product, contraction of the sample dimensions is so significant (see Fig. 4), as a result maximum of density and minimum of sample length are reached at 1100 °C.

SEM data of the sample annealed at 1100 °C (Fig. 7) reveals porous ceramics with rather homogeneous microstructure. Such a microstructure suites well the criteria stated at the beginning of the work and it is the basis to

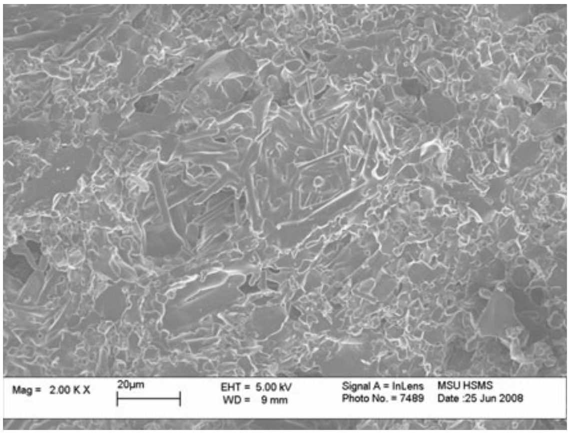

Fig. 7 HAp-based ceramics sintered at 1100 °C

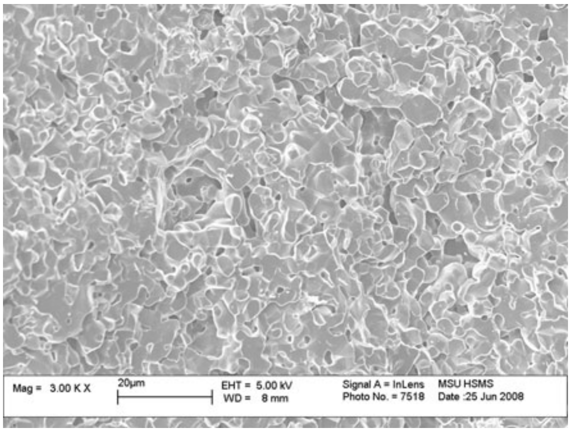

Fig. 8 Composite sample based on the brushite–HAp mixture, annealed at 1100 °C

recommend this material for detailed biomedical testing. It is worth noting that in this particular case of composite sample, liquid-phase sintering does not cause abnormal grain growth (as it can be seen in Fig. 6 for the HAp ceramics). We have to conclude that a possible reason for grain growth hindering could be the main interaction HAp + CPP → TCP. Nucleation of TCP phase due to the interaction at grain boundaries, cause pinning of a grain boundary to a nucleus of TCP and, thus, hamper grain boundary movement. This phenomenon facilitates overall densification of the ceramics and prevents coarsening of residual pores into large clusters (Fig. 8).

Conclusions

In this work, we obtained porous ceramics based on TCP. Ceramics is free from toxic components and will be subjected to further studies in vitro and in vivo. Using thermal analysis and XRD on annealed samples, we described full sequence of phase transformations in the material in the course of sintering of the ceramics. The main interaction of HAp + CPP → TCP type in the composite sample HAp/brushite takes place at temperatures higher than 700 °C and leads to rather uniform porous microstructure. Study of the composite samples (as well as brushite-based ceramics) gave an evidence that at 400–500 °C phases of $K_2CaP_2O_7$ and $Ca_5(PO_4)_3Cl$ appear, at 700–800 °C—phase of β-$Ca_3(PO_4)_2$. The role of KCl by-product consists in (i) it replace in part Ca in CPP phase making last one more reactive, (ii) it switches sintering of the ceramics in liquid-phase regime, (iii) at higher temperature it evaporates and, thus, contributes to formation of pores in the ceramics.

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