Biocompatible Ceramics for Implants Based on Calcium Phosphates

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ABSTRACT

The biocompatible ceramics containing calcium pyrophosphate $Ca_2P_2O_7$ (β-CPP), as biodegradation phase, has been studied. The data concerning the effect of HAp/monetite (or, CPP) mixture composition on powder compaction and subsequent sintering are presented. The influence of various parameters in microstructure of ceramic composites (HAp/$Ca_2P_2O_7$ (β-CPP)) is discussed.

Ceramic materials have been made from mixtures of stoihiometric hydroxyapatite (Hap) powders (Ca/P=1.67) and monetite ($CaHPO_4$, Ca/P=1). Powders of nanosized HAp and monetite were synthesized by means of wet precipitation from aqueous solutions of $Ca(NO_3)_2{*}4H_2O$ and $(NH_4)_2HPO_4$ at 60°C and pH=9 for HAp and pH=4-5 for monetite. Component ratio HAp:monetite was varied from 0:100 to 100:0 % with a step of 20% to adjust the level of bioresorption. Powders of raw materials and their mixtures were tested by means of XRD, TG, DTG, SEM, dilatometry. Linear shrinkage, density and microstructure of samples of the ceramics sintered in isothermal conditions at 900, 1000, 1100˚C with the time of holding up to 6 hours were tested.

Complicated consequence of phase transformations were established when the mixtures were heated from 20 to 1200°C. The CPP (Ca/P=1, converted from $CaHPO_4$ at 400-500˚C) reacts with HAp (Ca/P=1.67) and causes an additional weight loss in the region of 600-1050˚C due to solid state reaction leading to tricalcium phosphate (TCP, Ca/P=1.5) formation. Linear shrinkage of HAp compacts at 1100˚C after 6 hours was found to be about 21%; while for $Ca_2P_2O_7$ formed from monetite, and for the other mixtures - less than 11%. The fabricated ceramics with the phase composition of HAp, CPP and TCP, i.e. with a different content of a degradable phase and different ratio of CPP/TCP, can be treated as a biocompatible bioactive material with a tunable rate and limit of biodegradation.

INTRODUCTION

Biocompatible ceramics based on calcium phosphates are known to be a prospective material for biomedical applications. HAp ($Ca_{10}(PO_4)_6(OH)_2$), TCP ($Ca_3(PO_4)_2$) and CPP are used in clinical medicine due to their biocompatibility [1]. The materials consisted of 100 % phase of HAp have got the highest bioresistance among calcium phosphates. To control the level of biodegradability, the materials should consist of both stable HAp phase and bioresorbable phase. TCP based ceramics or glasses in systems CaO-P_2O_5-M_2O and CaO-P_2O_5-SiO_2-M_2O, where M=Na, R [2] are the most studied materials among bioresorbable ones. To the best our knowledge ceramic composites containing CPP is not under intensive consideration. The reason underlying such a fact is related explicitly to CPP deposits found in bone joints of patients suffering from arthritis due to wrong metabolism. Meanwhile, pyrophosphate-like unit is the main structural part of bisphosphonates [3], that are the basic ingredient of the row of medical drugs for treating osteoporosis and pancreatic diabetes [4].

HAp and other complex calcium phosphate salts are the end-products of biological mineralization process. Calcium pyrophosphate, $Ca_2P_2O_7$ (β-CPP), is thought to be one of the intermediate products involved in such process. The biological response with respect to new bone formation is quite similar for CPP and HAp. It was recognized recently, that sintered CPP causes better biological responses than pure Hap ceramics, so it has a great potential as a biodegradable bone substitute [5].

Several routes to generate CPP phase in ceramics can be assumed. CPP, as a second phase, may come from the frit (CaO-P_2O_5, Ca/P=0.2-0.75) used as a sintering additive in the course of liquid phase sintering of HAp powders [6]. Ceramics can be fabricated from powder of CPP with $Na_4P_2O_7$ [7] as a sintering additive, via interaction between H_3PO_4, or $(NH_4)_2HPO_4$, and porous HAp at high temperature after soaking it in solutions of the former ingredients [8]. Materials containing CPP can be either made from HAp chemically bonded with phosphoric or pyrophosphoric acids [9]. Finally, CPP can be formed by means of crystallization of glasses in the system CaO-P_2O_5 (the conversion of $CaHPO_4$ *$2H_2O$ or $CaHPO_4$ being heated to 400-700 °C is also to be taken into account) .

There are three polymorphs of CPP: β-$Ca_2P_2O_7$ — tetragonal, α-$Ca_2P_2O_7$ — monoclinic [10]; γ-CPP is converted to β-$Ca_2P_2O_7$ in the interval of 700-800^{0}C. β-$Ca_2P_2O_7$ is stable up to at least 1000^{0}C. According to some data in presence of HAp this phase can remain in ceramics after cooling [11].

Bearing in mind a great potential of CPP as biodegradable specie, it is worth noting that the rate of biodegradation depends also on: (i) materials texture (porosity type and level), (ii) nature of biodegradation phase (phase composition, grain size, properties of grain boundaries). The aim of the present work was focused on fabrication of multiphase ceramics with enhanced resorption caused by the presence of CPP phase and investigation of processes leading to formation of the multiphase ceramics based on HAp and CPP originated from $CaHPO_4$.

EXPERIMENT

Ceramic materials were prepared from powder mixtures of stoihiometric HAp (Ca/P=1.67) and monetite ($CaHPO_4$, Ca/P=1). Powders of HAp and monetite were synthesized by means of wet chemical precipitation from aqueous solutions of $Ca(NO_3)_2$*$4H_2O$ and $(NH_4)_2HPO_4$ at 60 C at pH=9 for HAp according to the reaction (1) and at pH=4-5 for monetite according to the reaction (2).

$$10Ca(NO_3)_2+6(NH_4)_2HPO_4+8NH_4OH=Ca_{10}(PO_4)_6(OH)_2+20NH_4NO_3+6H_2O \quad (1)$$
$$Ca(NO_3)_2 + (NH_4)_2HPO_4 + 2H_2O = CaHPO_4{\cdot}2H_2O\downarrow + 2NH_4NO_3 \quad (2)$$

The ratio HAp:monetite was varied from 0:100 to 100:0 % with a step of 20% (table 1). The precursors were mixed and disaggregated in a planetary mill with acetone as liquid media. Ceramic samples were sintered at 900, 1000, 1100˚C with isothermal holding up to 6 hours. As-received powders and the mixtures of them were tested by XRD, TG, DTG (Perkin Elmer Pyris, Perkin Elmer, USA), FESEM (LEO SUPRA-50VP Zeiss, Germany), dilatometry (DIL 402 PC –

1200°C, NETSCH, Germany). Linear shrinkage, density and microstructure of samples of sintered ceramic materials were studied.

Table 1. Composition of the mixtures.

Sample #	Initial content of the components		Phase composition of the mixtures according XRD	
	HAp pH=9	monetite pH=5	Before heat treatment	After heat treatment at 1100°C (6 hours)
1	100	0	HAp, NH_4NO_3	HAp
2	80	20	HAp, monetite	HAp, β-TCP
3	60	40	HAp, monetite	HAp, β-TCP, β-CPP
4	40	60	HAp, monetite	HAp, β-TCP, β-CPP
5	20	80	HAp, monetite	β-TCP, β-CPP
6	0	100	monetite, NH_4NO_3	β-CPP

DISCUSSION

According to XRD the as-received powders are consisted of the calcium phosphate (HAp and/or monetite) and ammonium nitrate. According to TG analysis the weight loss at about 200^{0}C related to a decomposition of ammonium nitrate was detected. The weight loss of monetite sample at 400-500°C corresponds to a conversion of monetite to CPP (equation 3).

$2CaHPO_4=Ca_2P_2O_5 + H_2O$ (3)

According to TG analysis of a mixture of HAP and CPP (fig.1), first three stages of the weight loss can be sequentially attributed to: 1) release of adsorbed and structural water from HAp, monetite and residual brushite $CaHPO_4{*}2H_2O$, 2) decomposition of ammonium nitrate, and 3) conversion of monetite into CPP. Significant weight loss in the interval of 600 - 1050^{0}C can be explained by interaction between HAp and monetite phases and formation of TCP.

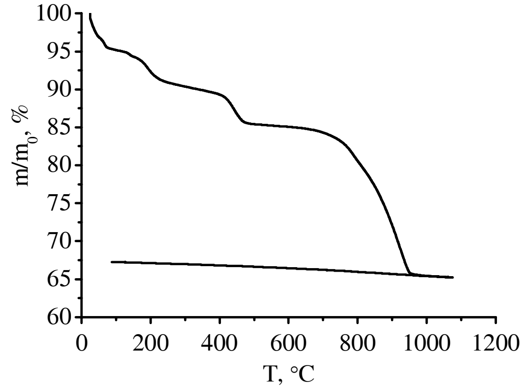	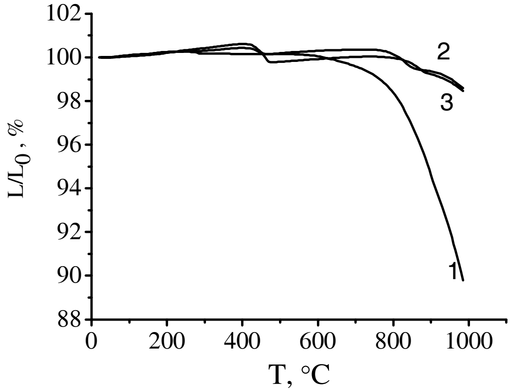
Fig. 1. TG of Hap/monetite powder mixture (the sample 3)	Fig.2. Liner shrinkage curves for the sample 1 - 100% HAp (1), the sample 6 - 100% monetite (3), and for the sample 3 – the mixture 60% HAp/40% monetite (2).

Linear shrinkage curves (fig. 2) for green compacts (pressed under 100 MPa) of the mixtures 1, 3 и 6 (see table 1) noticeably differ from each other. The fist step of the weigh loss on the pure HAp curve is relared to melting and decomposition of ammonium nitrate at about 250^0C, the second step is attributed to densification which starts at 600^0C. The change of the linear sizes of the samples after 600^0C could be explained by pore removal and densification, i.e. corresponds to the initial stage of sintering of HAp ceramics. One could detect two steps in the case of pure monetite sample. In this case the fist step is undoubtedly related to the transformation of monetite into CPP at 450 - 550^0C. The second step at 800 - 930^0C is supposed to be a fist stage of sintering of CPP. The character of a shrikage curve for the composition, containing green compact of HAp and monetite (HAp/CPP after 450-500^0C) is rather close to monetite (CPP) curve. It is likely that plate morphology of the CPP particles, inherited from monetite, prevents effective shrinkage of the mixture inspite of the presence of HAp particles being active to sintering.

Phase composition of the samples 1, 3, 6 after sintering at 1100^oC (6 hours) is presented in table 1. Three phases were found after sintering in case of the samples initially consisted of monetite and HAp: HAp, CPP and TCP. Such a fact is in a good agreement with TG data (fig.1). According to data [1] β-$Ca_3(PO_4)_2$ (β-ТКФ) is a high temperature phase, which can be synthesized only via solid state reactions. In this work the reaction between CPP (Ca/P=1) and HAp (Ca/P=1,67) partially takes place:

$$Ca_{10}(PO_4)_6(OH)_2 + Ca_2P_2O_7 \rightarrow 4Ca_3(PO_4)_2 + H_2O\uparrow \quad (4)$$

The microstructures of ceramics (samples 1, 3, 6) after sintering at 900, 1000 and 1100^oC for 6 hours are presented in figures 3-5. The microstructure of 100%-HAp ceramics is typical for under-sintered material, it contains numerous pores and corresponds to 88% of relative density (table 2). The 100%-HAp ceramics with relative density of 94% can be obtained by sintering at 1200^oC for 6 hours. The material of the composition 1 (100% HAp) demonstrates a maximal value of linear shrinkage (13%, 16% and 21 % after sintering at 900, 1000, 1100^oC, respectively) in contrast to the rest compositions. The microstructure of the sample 6 (100% CPP) consists of large grains of 20-30 μm. The microstructure of multiphase ceramics (composition 3, i.e. HAp/TCP/CPP) differs from those ones corresponding to the materials formed only from HAp or CPP. One can see grains of CPP (3-5 μm), under-sintered areas of HAp (size of particles less than 1 μm), as well as grains of TCP (size of particles of about 1 μm), formed in gaps between CPP and Hap grains. The arrangement of the phases over the samples and the grain size distribution give an evidence of the sintering mechanism, being accompanied by a solid state reaction of TCP formation, which inhibits a grain growth of CPP.

According to the work [12], β-CPP in amount of 0,5-3% wt. can stabilize the phase β-TCP at least up to 1200^oC and, therefore, can be used as an additive allowing to carry on an annealing at temperature higher than that possible for the ceramics based on TCP.

Table 2. Relative density of the samples after sintering at different temperatures (6 hours)

Sample #	Initial composition of the mixtures	Relative geometrical density, %		
		900^0C	$1000\ ^0C$	$1100\ ^0C$
1.	HAp 100%	66,5	70,1	88,2
3.	HAp 60% + монетит 40%	53,1	55,9	71,3
6.	monetite 100%	59,9	77,1	80,1

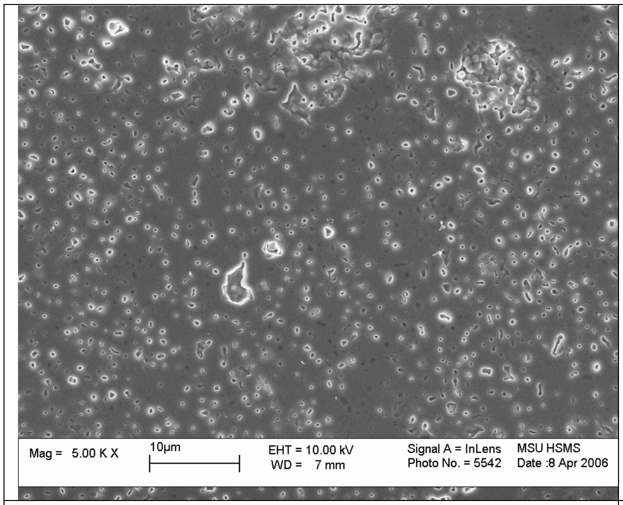

Fig.3. SEM micrograph of the sample 1 after sintering at 1100^{0}C (6 hours).

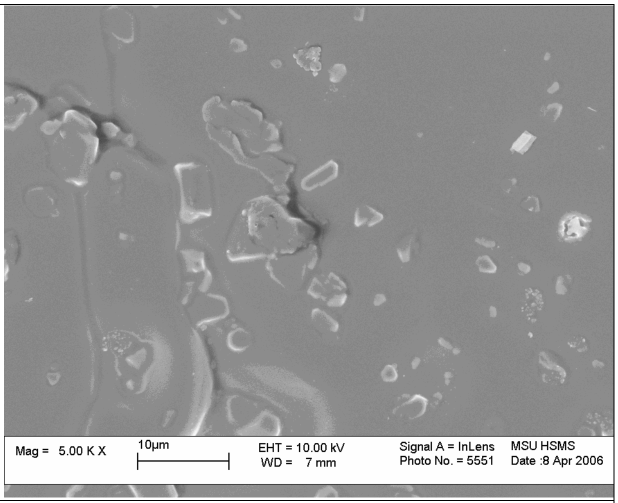

Fig.4. SEM micrograph of the sample 6 after sintering at 1100^{0}C (6 hours).

The values of relative density of the ceramics (samples # 2-5) after sintering at 900, 1000, 1100 ^{o}C are within 1.49-2.10 g/cm^3, 1.53-2.25 g/cm^3 1.95-2.81 g/cm^3, respectively. The values are lower in comparison with those for single phase ceramics consisted only of HAP or CPP (table 2). Density of the composites depends on a row of factors: phase composition, peculiarities in micromorphology of phases(HAp, TCP and CPP), the presence of very special by- products such as ammonium nitrate, phase transition in CPP, phase transformations accompanying sintering process (HAp + CPP → TCP) etc.

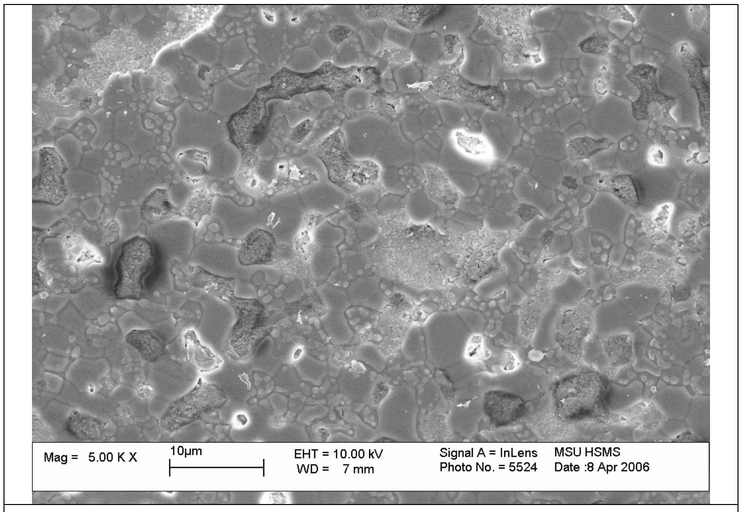

Fig.5. SEM micrograph of the sample 3 after sintering at 1100^{0}C (6 hours).

CONCLUSIONS

Complicated consequence of phase transformations takes place during heating the mixtures of HAp and monetite from 20 to 1200 °C. The CPP (Ca/P=1, converted from $CaHPO_4$ at

400-500˚C) reacts with HAp (Ca/P=1.67) leading to TCP (Ca/P=1.5) formation. Linear shrinkage of HAp compacts at 1100˚C after 6 hours was found to be about 21%; while for $Ca_2P_2O_7$ formed from monetite,and for their mixtures - less than 11%. Resulted ceramics with the phase composition of HAp, CPP and TCP, i.e. with a different content of degradable phase and different ratio of CPP/TCP, can be regarded as a biocompatible bioactive material with a tunable limit of biodegradation.

ACKNOWLEDGMENTS

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