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Mechanical properties of bovine hydroxyapatite (BHA) composites doped with SiO_2, MgO, Al_2O_3, and ZrO_2

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Abstract Biologically derived hydroxyapatite from calcinated (at 850 °C) bovine bones (BHA) was doped with 5 wt% and 10 wt% of SiO_2, MgO, Al_2O_3 and ZrO_2 (stabilized with 8% Y_2O_3). The aim was to improve the sintering ability and the mechanical properties (compression strength and hardness) of the resultant BHA-composites. Cylindrical samples were sintered at several temperatures between 1,000 and 1,300 °C for 4 h in air. The experimental results showed that sintering generally occurs at 1,200 °C. The BHA–MgO composites showed the best sintering performance. In the BHA–SiO_2 composites, extended formation of glassy phase occurred at 1,300 °C, resulting in structural degradation of the resultant samples. No sound reinforcement was achieved in the case of doping with Al_2O_3 and zirconia probably due to the big gap between the optimum sintering temperatures of BHA and these two oxides.

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Introduction

The number of grafting procedures steadily increases nowadays. Therefore, there is an urgent need for finding effective ways for enhancement of bone formation [1] after a restoration operation via developing low cost biomaterials with controlled biocompatibility [2]. Hydroxyapatite (HA, $Ca_{10}(PO_4)_6(OH)_2$) materials are very popular for bone restorations because they accelerate bone growth around the implant due to their chemical and crystallographic similarity to human carbonated apatite [3]. Biomaterials of synthetic HA are highly reliable but the synthesis of HA is often complicate and expensive. Bioceramics of naturally derived biological apatites are more economic. Moreover, Mother Nature herself has endowed them with specific substitutions at the Ca^{2+}, PO_4^{3-} and OH^- sites of HA lattice as well as with several trace elements, which may play an important role in the physiological functioning and osseointegration process. Nevertheless, biologically derived HA can also bear fatal diseases, such as human immunodeficiency virus (HIV) or bovine spongiform encephalopathy (BSE). We have discussed safety issues for biomaterials of biological HA in our recent publications [2, 3].

The applications of pure HA are restricted to non load-bearing implants due to the poor mechanical properties of

HA [4]. Doping with (biocompatible or even better bioactive) oxides may result in strong HA composites [5]. In this study, we have doped biologically derived HA from bovine bones (BHA) with (5 and 10 wt%) SiO_2, MgO, Al_2O_3, and zirconia.

The oxides SiO_2 and MgO are related to bioactivity. Silicon is related to body's metabolism, clinically proven in studies on bone and collagen weakening, the level of arteriosclerosis, osteoarthritis, aging process etc. [6]. In -vivo tests have shown that silicon-substituted HA promotes early bonding at bone/implant interface [7]. Good results have been also obtained in cell culture studies using 2% SiO_2 [8].

Magnesium is also a very important element in human body [9, 10], related to mineralization of calcined tissues, apatite crystallization, destabilization of HA and the thermal conversion of HA to β-tricalcium phosphate (β-TCP, $Ca_3(PO_4)_2$). Magnesium seemingly reduces risks of cardiovascular diseases, promotes catalytic reactions and controls biological functions. Good results have been obtained in cell culture studies using 1% MgO [8]. Mg-containing HA composites have been suggested in biomedicine, such as bredigite ($Ca_7MgSi_4O_{16}$, considered as similarly bioactive to CaO–SiO_2 [11]) [12], forsterite (Mg_2SiO_4) and enstatite ($MgSiO_3$ [13], considered as machineable biomaterial [10]).

The oxides Al_2O_3 [14, 15] and zirconia [16, 17] are typical representatives of inert bioceramics [18] with remarkable mechanical performance. Therefore, the tested composites of HA doped with these two oxides aimed to potentially enhance the mechanical properties of HA with maintenance of HA bioactivity. With regard to zirconia, 3% yttria stabilized ZrO_2 has attracted the most of interest while 8% yttria stabilized ZrO_2 was mostly used in plasma-spray coatings.

Materials and experimental procedure

The BHA powder used in this study was obtained from calcinated fresh bovine femurs, according a method described earlier [19]. In brief, the heads of fresh femurs were cut off. The obtained shafts were deproteinized with NaOH and, after washing, calcinated at 850 °C for 4 h in air. Then, they crashed and ball milled until fine powder was obtained (mean particle size 5–10 μm). High purity fine commercial powders of SiO_2, MgO, Al_2O_3 and ZrO_2 (stabilized with 8% Y_2O_3) were used.

The fine powders of the doping oxides were mixed with the fine powder of BHA in a way that the final mixtures contained 5 and 10 wt% of the doping oxide. The mixtures were well homogenized by ball milling. Pellets (6 mm diameter, 12 mm height) were prepared by uniaxial cold pressing in hardened steel dies, according to British Standards (No. 7253). The pellets were sintered at different temperatures between 1,000 and 1,300 °C for 4 h in air. The heating and the cooling rates were 4 K/min.

The compression strength of the obtained samples was measured with an Instron apparatus (UK, 2 mm/min displacement). For the measurements of Vickers microhardness, an Instron 2100 microhardness tester was employed (200 g load was applied for 20 s). The apparent density of the samples was measured by the Archimedes method (i.e. immersion in ethanol). To estimate the mean values and the standard deviations of each property ten (at least) different samples were tested. The microstructure of the samples was observed by field emission scanning electron microscopy (FE-SEM Hitachi S-4100, Japan; 25 kV acceleration voltage, beam current 10 μA), equipped with energy dispersive spectroscopy (EDS) for elemental chemical analysis. The crystalline structure of the samples was determined with X-ray diffraction analysis (XRD, Rigaku Geigerflex D/Mac, C Series, CuKα radiation, Japan).

Results

Table 1 summarizes the experimental results of compression strength (σ), Vickers microhardness and density of the samples sintered at different temperatures. An overview of these values generally suggests that the samples heat treated at the lower tested temperatures were poorly sintered, while sintering considerably improved at the higher temperatures.

SEM observations support that conclusion. Figure 1 shows the evolution of microstructure of BHA composites over increasing sintering temperature (1,000 °C Fig. 1a, e; 1,100 °C Fig. 1b, f; 1,200 °C Fig. 1c, g; 1,300 °C Fig. 1d, h) for the cases of 5% SiO_2 (Fig. 1a–d) and 5% MgO (Fig. 1e–h) doping. Similar microstructures were generally observed for the cases of Al_2O_3 and zirconia doping. Evidently, many small particles were poorly connected one to the other at the lower temperatures (usually 1,000 and 1,100 °C, Fig. 1a, b, e, f), while fusion of grain boundaries and extensive formation of glassy phase, which wets the particles and closes the pores, resulted in dense bulk samples at higher temperatures (usually 1,200 and 1,300 °C, Fig. 1c, d, g, h).

Furthermore, the high values of microhardness of the samples sintered at 1,000 °C (Table 1) rather represent the hardness of the initial materials than those of a sintered body of a composite material. On the other hand, the values of microhardness of the samples sintered at 1,300 °C resemble values of glasses [18], which support extensive formation of glassy phase during sintering at the higher tested temperatures.

Table 1 Mechanical properties and density of the investigated HA-composites (the SD of the density measurements was <5%; NA: Not applicable)

Oxide	T (°C)	σ (MPa)		Hardness (HV)		Density (g/cm^3)	
		5%	10%	5%	10%	5%	10%
SiO_2	1,000	52.63 ± 6.04	45.93 ± 3.69	111 ± 5	19 ± 2	2.88	2.80
	1,100	62.68 ± 13.74	56.54 ± 3.76	64 ± 2	71 ± 1	2.84	2.74
	1,200	79.09 ± 11.12	74.86 ± 5.07	93 ± 4	91 ± 4	2.70	2.73
	1,300	9.86 ± 1.76	37.72 ± 6.77	224 ± 8	NA	2.29	2.68
MgO	1,000	31.77 ± 9.54	23.90 ± 2.47	55 ± 1	14 ± 1	2.88	2.56
	1,100	36.96 ± 5.70	39.05 ± 4.72	81 ± 4	101 ± 4	2.84	2.70
	1,200	61.09 ± 6.57	61.09 ± 6.57	147 ± 2	168 ± 7	2.83	2.87
	1,300	121.85 ± 7.00	98.23 ± 7.10	305 ± 16	218 ± 12	2.84	2.82
Al_2O_3	1,000	44.60 ± 1.66	26.97 ± 2.90	159 ± 2	44 ± 5	2.61	2.86
	1,100	62.23 ± 2.14	38.99 ± 3.65	70 ± 6	114 ± 6	2.67	2.97
	1,200	72.85 ± 1.81	54.36 ± 5.71	85 ± 4	81 ± 6	2.88	2.57
	1,300	77.45 ± 4.79	87.81 ± 26.29	450 ± 16	250 ± 28	2.75	2.90
ZrO_2	1,000	23.02 ± 5.49	24.32 ± 0.55	86 ± 30	69 ± 16	3.03	3.09
	1,100	41.81 ± 1.72	39.01 ± 4.56	94 ± 10	103 ± 37	2.99	3.04
	1,200	45.47 ± 0.09	46.58 ± 1.94	170 ± 28	127 ± 20	2.76	3.00
	1,300	48.45 ± 0.58	56.96 ± 6.01	256 ± 23	154 ± 6	2.73	2.75

With regard to the evolution of crystalline phases over increasing sintering temperature, no extra phases were generally detected, related to the doping oxides, after sintering at temperatures up to 1,200 °C. The typical diffractograms of Fig. 2a, which correspond to the 10% MgO–BHA composites sintered at different temperatures, confirm that general trend. The formation of glassy phase, especially at 1,200 and 1,300 °C, is also confirmed in these diffractograms. XRD peaks of TCP and phases associated to the doping oxides (for instance $Ca_{10}(PO_4)_4(SiO_4)_2$ for the case of SiO_2, etc.) became more evident after sintering at 1,300 °C, together with considerable decrease of crystallinity (see Fig. 2b for the case of 10% zirconia doping).

Beyond the above general trends, the values of Table 1 reveal also several peculiarities among the investigated composites. The HA-SiO_2 composites sintered at 1,300 °C featured a dramatic decay of compressive strength and densification (in a second attempt for the case of 5% SiO_2, we measured $\sigma = 13.65 \pm 0.83$ MPa). In the case of 10% SiO_2, the appearance of the sintered sample resembled rather a baked cake than a dense sintered body. Figure 1d shows an extended formation of glassy phase for the case of 5% SiO_2 doping and 1,300 °C (comparing to Fig. 1h of 5% MgO doping). The microstructure of 10% SiO_2–BHA, sintered at 1,300 °C, presented in Fig. 3, shows that the large amount of glassy phase, after cooling, resulted in an extensive network of cracks, which should be responsible for the structural collapse of the samples with that composition. Figure 2c shows that a highly crystalline regime characterizes the BHA–SiO_2 composites sintered at 1,200 °C (for both 5 and 10% doping) but the SiO_2 content strongly influences the crystallinity of the resultant BHA-SiO_2 composite after sintering at 1,300 °C.

The BHA–MgO composites exhibited an ideal behaviour, following the general trend of poor sintering at lower temperatures and good sintering at higher temperatures. However, the best mechanical properties were obtained with 5% MgO doping than with 10% MgO.

In comparison with SiO_2 and MgO doped BHA, the incorporation of bioinert oxides (Al_2O_3 and zirconia) in BHA seemingly lowers sintering temperatures from 1,200 to 1,100 °C (see the values of Table 1). Nevertheless, there was not an outstanding increase of the maximum achieved mechanical properties at higher temperatures. SEM observation of the sintered samples found that these doping oxides were often concentrated in large spots. Figure 4 shows these spots for the case of zirconia doping (10%, 1,300 °C). EDS point analysis at these spots measured high concentrations of zirconium (9–17%).

Discussion

Incorporation of specific elements in HA lattice is directed by Mother Nature. Enamel, dentin and bone contain 0.44, 1.23 and 0.72 wt% of magnesium, respectively [20]. Tooth enamel exhibits higher strength than bone HA because of the higher F-content. Regarding the derived composites, Genc et al. [21] prepared HA-zirconia composites using human enamel HA (instead of BHA) and found higher

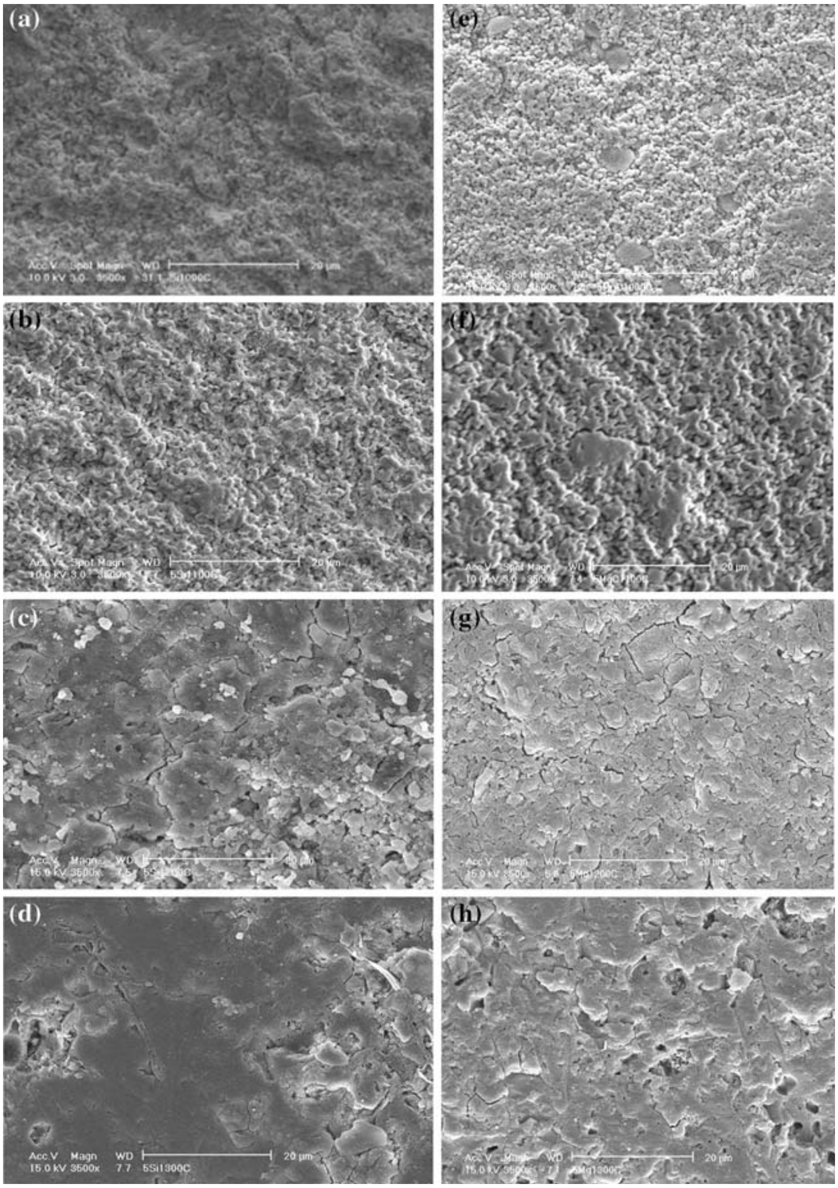

Fig. 1 Microstructure of BHA composites doped with 5% SiO_2 (**a**–**d**) and MgO (**e**–**h**) sintered at 1,000 °C (**a**, **e**), 1,100 °C (**b**, **f**), 1,200 °C (**c**, **g**) and 1,300 °C (**d**, **h**) for 4 h in air

values of compressive strength than in the present study (i.e. 1,200 °C: 65 MPa for 5% ZrO_2 and 82 MPa for 10% ZrO_2; 1,300 °C: 86 MPa for 5% ZrO_2 and 97 MPa for 10% ZrO_2). Beyond the benefits of biological origin and low production cost of BHA, the production method of BHA in the present study anticipates high safety, since the high temperature of calcination (850 °C) eliminates all risks of transmitting fatal deceases [2].

The experimental results of the present study (Table 1) are evaluated in the light of results of earlier similar studies for pure BHA, presented in Table 2 [22–24], and doped BHA with 5 and 10% TiO_2 [4] and zirconia (stabilized with 3% yttria) [16], presented in Table 3. Accordingly, except the case of zirconia, doping with oxides generally seems as a promising way for producing HA-composite biomaterials with a potential in load bearing biomedical applications.

Regarding the mechanism of sintering, the mixture of BHA with the doping oxides seemingly possesses the individual characteristics of the mixing phases at 1,000 °C. Sintering is still rather poor also at 1,100 °C. Evidences of diffusion and sintering occurrence with the formation of glassy phase [25] are observed at 1,200 °C. The formation of glassy phase certainly depends on the phase diagrams which govern the local HA-oxide equilibria at the grain boundaries, which undergo fusion at a certain temperature. Regarding the features of these phase diagrams, the results of X-ray analysis suggest that the cations of the doping oxides, when their concentration is up to 10 wt%, are smoothly incorporated in the lattice of HA at temperatures

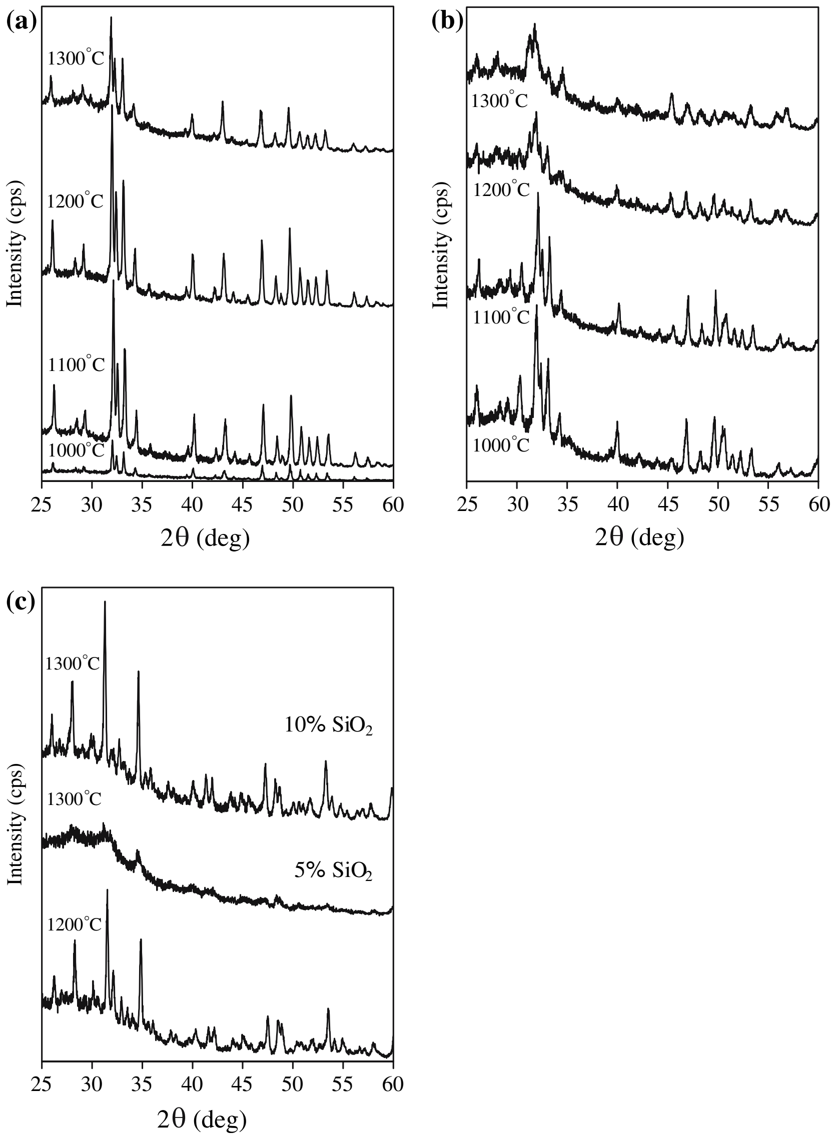

Fig. 2 X-ray diffractograms of BHA composites doped with (**a**) 10% MgO, (**b**) 10% zirconia and (**c**) SiO_2, sintered at different temperatures for 4 h in air

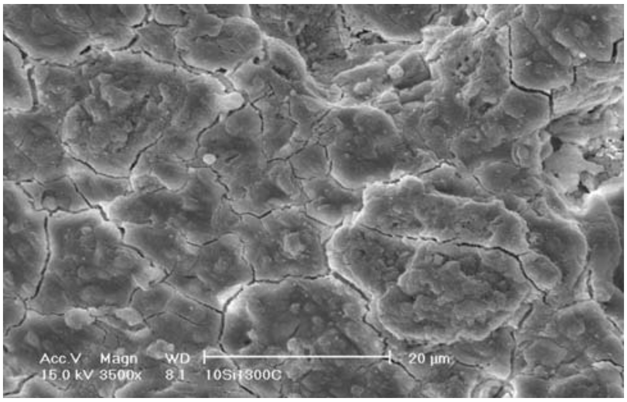

Fig. 3 Overfiring caused extensive cracking in samples of BHA doped with 10% SiO_2 sintered at 1,300 °C for 4 h in air

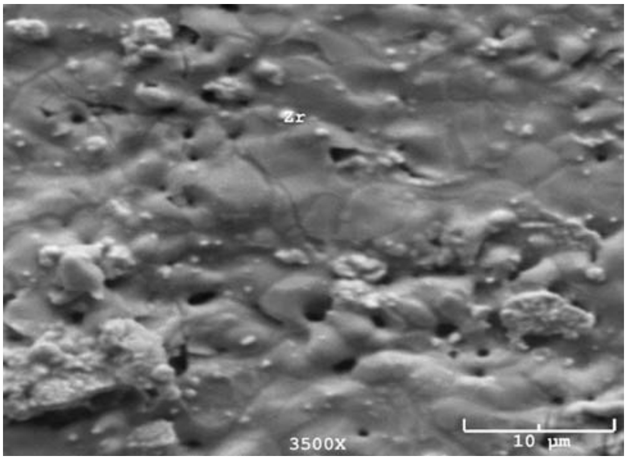

Fig. 4 Visible large spots (see the white patches) of zirconia on the surface of BHA samples doped with 10% zirconia sintered at 1,300 °C for 4 h in air

Table 2 Mechanical properties of samples of pure BHA measured in earlier studies [22–24]

T (°C)	σ (MPa)		Hardness (HV)	
	[22–23]	[24]	[22–23]	[24]
1,000	48 ± 20	12 ± 2	85 ± 9	42 ± 2
1,100	22 ± 5	23 ± 3	74 ± 20	92 ± 4
1,200	75 ± 18	67 ± 7	148 ± 10	138 ± 3
1,300	65 ± 42	62 ± 11	131 ± 18	145 ± 3

Table 3 Mechanical properties of BHA-composites reinforced with TiO_2 [4] and zirconia (3% Y_2O_3 stab.) [16] measured in earlier studies

Oxide	T (°C)	σ(MPa)		Hardness (HV)	
		5%	10%	5%	10%
TiO_2 [4]	1,000	26 ± 1	61 ± 1	58 ± 2	74 ± 4
	1,100	43 ± 1	48 ± 1	69 ± 3	135 ± 7
	1,200	86 ± 2	104 ± 4	144 ± 4	180 ± 9
	1,300	105 ± 4	89 ± 6	204 ± 19	247 ± 11
ZrO_2 [16]	1,000	22 ± 3	24 ± 5	59 ± 4	72 ± 2
	1,100	36 ± 5	32 ± 6	66 ± 1	91 ± 2
	1,200	32 ± 6	46 ± 12	134 ± 5	144 ± 1
	1,300	45 ± 8	50 ± 10	166 ± 2	145 ± 1

up to 1,200 °C. It would be interested to calculate the changes of HA lattice due to the incorporation of these cations as a function of temperature and the content of the doping oxide. However, such a study would have a quantitative reliability only if it would be done with highly pure synthetic HA. The biologically derived BHA has intrinsically and inevitably cation incorporations (trace elements and substitutions), often random, already in HA lattice. The formation of crystalline phases associated to the doping oxides in the samples heat treated at 1,300 °C should be attributed to the extensive formation of glassy phase (which, during cooling, precipitates these phases), the transformation of HA to TCP (whereby, there is different capability of TCP for accommodating foreign ions in its lattice than HA) and the sizes of the cations of the different oxides tested in this study.

The formation of glassy phase certainly aids sintering. Nevertheless, in the case of the BHA–SiO_2 composites, it resulted in typical over-firing effect after firing for 4 h at 1,300 °C, which means that the extensive formation of glassy phase led to structural collapse of the sintered samples. Shorter heat treatment might reduce the extent of that detrimental phenomenon. The incorporation of MgO in BHA was considerably better and resulted in composites with remarkable resistance to over-firing effect. Doping with 5% MgO resulted in stronger materials than 10% MgO, suggesting that there should be an optimum amount of MgO (lower than 10%) for getting the strongest BHA–MgO composites. The higher capability of HA to accommodate bigger amount of Mg cations in its lattice than Si cations would be attributed to the difference of cation sizes. Beyond, however, influencing sintering and mechanical properties, the soluble glassy phase forms during sintering should have also an important effect in the in vitro and in vivo bioactivity performance of the produced composites [5, 26].

The incorporation of bioinert oxides was evidently less successful, regarding the demanded increasing of mechanical properties of the resultant composites, likely due to the poor distribution of the doping oxides in the sintered bodies. However, the presence of these oxides in large spots in the microstructure of the produced BHA-composites (Fig. 4) is welcome because they can act as crack arresters, reducing composites' brittleness. Furthermore, there is a big gap between the ideal sintering temperatures of BHA (1,200 °C, Table 2) and alumina (1,600 °C) and zirconia (1,550 °C). Hence, these oxides should be incorporated in the lattice of HA already from the production stage. This is easily possible in the case of synthetic HA, via sol–gel or co-precipitation chemical methods.

In earlier studies, considerably higher amounts of these oxides have been used (20% Al_2O_3 [27], 70 vol% ZrO_2–Al_2O_3 [28], 80–90 vol% Al_2O_3 [15], 7.58–32.89% ZrO_2 [29]), but it is questionable if those big amounts jeopardize the bioactivity of the resultant composites. In the case of zirconia, comparison of the present results (Table 1) with the results of Table 3 [16] suggests that the amount of yttria does not crucially affect the mechanical properties of the produced HA-zirconia composites. The poor mechanical properties of HA-zirconia composites may be related to the intrinsic transformation of zirconia to cubic crystalline structure [30].

Consequently, to anticipate controlled bioactivity and mechanical properties, the amounts of doping oxides have to be optimized. Suchanek et al. have proposed simultaneous doping of HA with many oxides (MgO, Al_2O_3, SiO_2, Li_2O) [20].

Conclusions

Doping of BHA with oxides is seemingly a promising way for improving its mechanical properties. In BHA-oxide composites, extended formation of glassy phase generally occurs at 1,200 °C, favouring sintering. To get the strongest composites, the formation of glassy phase should be controlled. This depends on the nature of the oxide (i.e. cation size), the sintering temperature and the compatibility of sintering temperatures between BHA (1,200 °C) and the doping oxide.

Doping with MgO resulted in the best sintering behaviour and strong and dense BHA composites, especially for 5% MgO. The use of SiO_2 should be carefully considered since over-firing effect (i.e. extensive formation of glassy phase) causes collapse of the resultant material after prolong (4 h) heat treatment at 1,300 °C. The incorporation of alumina and zirconia (stabilized with 8% Y_2O_3) did not result in very strong BHA-composites likely because of the big gap between the sintering temperatures of BHA and these two oxides.

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