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Liquid phase sintering of hydroxyapatite by phosphate and silicate glass additions: structure and properties of the composites

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Phosphate- and silicate-based glasses were added to hydroxyapatite in order to improve its mechanical properties and to fabricate composites with different degrees of bioactivity. A strong chemical bonding was obtained between hydroxyapatite and the phosphate-based glasses leading to samples approaching theoretical density, according to density measurements and scanning electron microscopy. Bioglass® additions led to the formation of a complex calcium phosphate silicate which hampered the reinforcement process. The fracture toughness of the hydroxyapatite–glass composites was shown to be within the 1.1–1.2 MPa $m^{1/2}$ range, which is double that determined for sintered hydroxyapatite. A 2 μm thick apatite layer was observed on the surface of the hydroxyapatite-glass composites after 48 h immersion in a simulated human blood plasma, whereas only a few apatite crystals were detected on sintered hydroxyapatite after 7 days immersion. From the results obtained we anticipate that the composites might show a higher rate of bone bonding, leading to enhanced bioactivity.

1. Introduction

Recent developments [1–7] in the design of bone replacement materials have been towards the use of materials which allow bone to grow and attach onto their surface. Hydroxyapatite (HA) has been extensively used but is limited to low-load applications [8–10]. There is a great need for producing materials with both different bioactivity and higher mechanical properties than sintered hydroxyapatite, as mechanical compatibility with the surrounding host tissue is an absolute requisite for a sound implant–tissue interface [8]. Glasses within the P_2O_5–CaO–Na_2O system have been considered as having an enormous potential as biomaterials [11–13], because their chemical composition is analogous to that of the inorganic constituent of the mineral part of bone. Their biocompatibility and bioactivity have also been demonstrated as being adequate [12, 14], especially as temporary space fillers [14]. Several attempts [15–19] have been made in order to reinforce hydroxyapatite and to approximate its mechanical properties to those of bone. Hydroxyapatite–polymer [17, 18] and glass–ceramic [15, 16] composites have probably been the most successful. However, both show a completely different microstructure from bone.

In this work, phosphate-based glasses were added to hydroxyapatite by a simple liquid phase sintering process. All ions added to the glass formulation were chosen taking into account the mineral part of bone, and therefore only Ca–P phases were found in the microstructure of these composites. Bioglass® was also added to compare the effect of a SiO_2-based glass on the sintering mechanism of hydroxyapatite.

2. Materials and methods

Three phosphate-based glasses, with the chemical compositions listed in Table I, were prepared from reagent grade chemicals (BDH Chemicals Ltd). Chemicals were placed in a platinum crucible and heated at 1300 °C for 1 h. Once the glass was poured, it was coarsely reduced to a sand-type particle and milled in a porcelain ball mill pot for 24 h. Methanol and

TABLE I Chemical composition (mol %) of phosphate-based glasses and Bioglass®

Glass addition	P_2O_5	CaO	Na_2O	Al_2O_3	SiO_2
2 oxide	45.5	54.5	–	–	–
3 oxide	45.0	28.0	27.0	–	–
4 oxide	62.9	10.1	10.1	16.9	–
Bioglass®	2.6	26.9	24.0	–	46.1

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TABLE II Chemical composition (g/dm^3) of the simulated human blood plasma

NaCl	KCl	$CaCl_2.2H_2O$	$NaHCO_3$	$K_2HPO_4.3H_2O$	$Na_2SO_4.10H_2O$	$MgCl_2.6H_2O$
8.0	0.22	0.37	0.35	0.30	0.16	0.30

hydroxyapatite were then added (350 cm^3 of methanol/200 g of hydroxyapatite) to wet mill the powders together for a further 24 h. In order to minimize phase changes, only 2.5 wt % of glass was added to hydroxyapatite. Powders were then dried and samples uniaxially pressed at 288 MPa, heated at 4 °C/min, and finally fired for 1 h at 1200 °C to 1350 °C. Hydroxyapatite–Bioglass® composites were also fabricated, using the same percentage of glass. Bioglass® was obtained from the Bioglass® Research Centre, University of Florida.

X-ray diffraction analysis (XRD) was performed in a Siemens D5000 diffractometer using CuK_α radiation at 40 mA and 40 kV. Scanning electron microscopy (SEM) analysis equipped with energy dispersive spectroscopy was used to analyse the microstructure of the composites. Grain size was determined by the linear intercept method after chemical etching with 10% citric acid solution, for 3–4 min at room temperature. A strength indentation technique was used to determine fracture toughness; this consists in making a Vickers indentation at the centre of the tensile surface of each material to precrack the samples, followed by a bending test. A concentric ring test [20] was then performed and k_{1c} was determined according to the process proposed by Chantikul [21], using the following equation:

$$K_{1c} = A(|E/H)^{1/8}(\sigma F^{1/3})^{3/4} \quad (1)$$

where K_{1c} is the fracture toughness, A a geometric constant, σ the strength of the pre-cracked sample, E the Young's modulus, H the hardness and F the load. Bioactivity tests were conducted to assess apatite layer formation in a simulated human blood plasma solution, at 37 °C, with the composition presented in Table II.

3. Results and discussion

The densification of hydroxyapatite was significantly enhanced by the presence of a liquid phosphate phase chemically related to its composition during its sintering process. Fig. 1 shows the microstructure of HA sintered at 1300 °C. Fig. 2 presents a light micrograph for HA-3 oxide glass composites sintered at the same temperature. It was not possible to find an etching procedure to prepare composite samples for SEM observation due to the much higher dissolution rate of TCP.

While the best densification obtained for the sintered hydroxyapatite compacts was 97% of the theoretical density of hydroxyapatite, for compacts sintered at 1300 °C, a density approaching 100% of the theoretical value was achieved for the hydroxyapatite–phosphate glass composites. Densification occurred by liquid formation and spreading, improving the diffusion mechanism. A strong bonding was developed between hydroxyapatite and the phosphate-based glasses, which acted on the solid hydroxyapatite particles reducing the interfacial energy and eliminating porosity. The presence of a solid hydroxyapatite skeleton (favouring heterogeneous nucleation), the slow cooling rate after sintering, and the tendency of hydroxyapatite to be transformed into tricalcium phosphate at high temperatures, led to the appearance of crystalline α and β tricalcium phosphate (TCP) structures, as was detected using X-ray diffraction and energy dispersive spectroscopy. The following general tendency of transformation with increasing sintering temperature was observed: hydroxyapatite → β-TCP → α- TCP. The amount of TCP present in the microstructure of the composites depended on the chemical composition of the glass added to hydroxyapatite, as was demonstrated in earlier works [22, 23]. With Bioglass® additions a lower degree of densification was achieved than with HA-phosphate based glass composites, as we have previously reported [23]. As a consequence, we may hypothesize

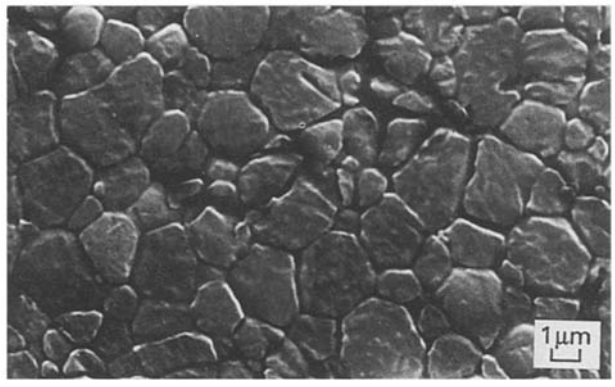

Figure 1 Microstructure for HA sintered at 1300 °C.

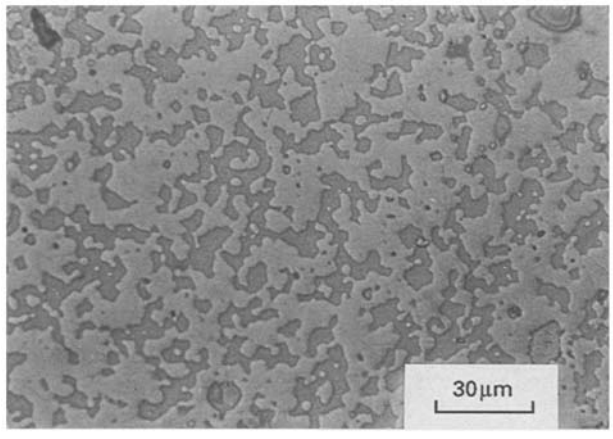

Figure 2 Microstructure for HA–3 oxide glass composite sintered at 1300 °C.

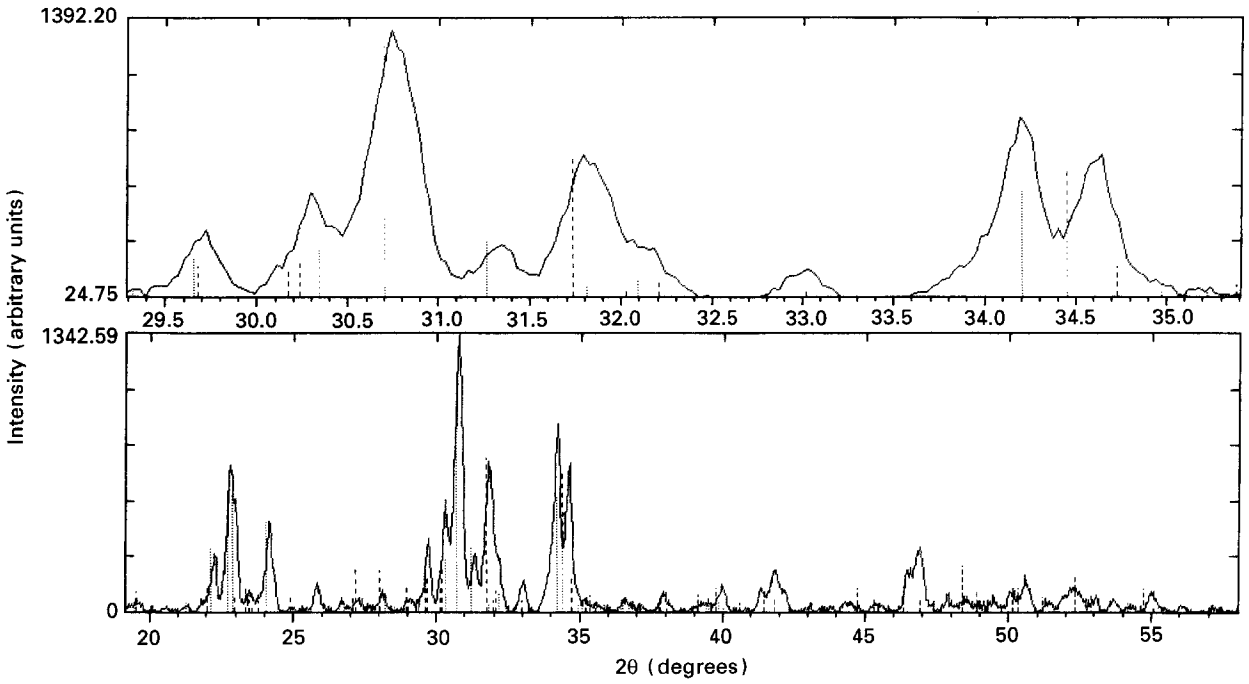

Figure 3 X-ray diffraction pattern for HA–Bioglass® composite sintered at 1350 °C (lower). Zoom of the main area, showing the matching between experimental pattern and standard file for calcium phosphate silicate (---) and calcium phosphate (·····).

TABLE III Fracture toughness results for sintered HA and HA–glass composites

Material	Fracture toughness ($MPa\ m^{1/2}$)		
	1250 °C	1300 °C	1350 °C
HA	0.41 ± 0.05	0.50 ± 0.02	0.30 ± 0.02
HA–2 oxide	0.63 ± 0.03	1.20 ± 0.05	0.62 ± 0.04
HA–3 oxide	0.72 ± 0.04	1.10 ± 0.05	0.61 ± 0.06
HA–4 oxide	0.75 ± 0.06	1.20 ± 0.06	0.93 ± 0.05
HA–Bioglass®	0.95 ± 0.06	0.95 ± 0.04	0.74 ± 0.03

TABLE IV Grain size measurements for sintered HA and HA–glass composites

Material	Grain size (μm)			
	1200 °C	1250 °C	1300 °C	1350 °C
HA	1.3 ± 0.2	2.4 ± 0.2	3.3 ± 0.4	8.4 ± 0.9
HA–2 oxide	0.7 ± 0.1	0.9 ± 0.1	1.2 ± 0.1	1.8 ± 0.1
HA–3 oxide	0.6 ± 0.2	0.7 ± 0.1	0.9 ± 0.1	1.6 ± 0.2
HA–4 oxide	0.7 ± 0.2	0.9 ± 0.1	1.1 ± 0.1	1.9 ± 0.2
HA–Bioglass®	0.8 ± 0.1	0.9 ± 0.1	1.2 ± 0.1	1.7 ± 0.2

that the Bioglass® did not develop such a strong bonding with hydroxyapatite, probably due to the presence of SiO_2. Calcium phosphate silicate was formed after sintering, as may be seen in the X-ray diffraction analysis of Fig. 3. This intermetallic compound seems to be responsible for some porosity in the microstructure, as reported previously [24].

The fracture toughness was significantly improved for hydroxyapatite–glass composites when compared to sintered hydroxyapatite, as shown in Table III. Values for samples sintered at 1200 °C were not considered because they did not have enough area free of porosity to make the indent.

k_1 values are two to three times higher than those for sintered hydroxyapatite. The maximum values were obtained for materials sintered at 1300 °C, followed by a decrease above this temperature, probably due to abnormal grain growth. The peak in toughness at 1300 °C should be attributed to the combination of a good densification with a small grain size. Grain size measurements are presented in Table IV.

The presence of the liquid phase inhibited the grain growth of hydroxyapatite, leading to small grain size structures. The higher densification obtained and the smaller grain size seem to be the main factors which contributed to the improvement in fracture toughness of these composites. In addition to these phenomena, it should also be mentioned that TCP has a slightly higher fracture toughness than HA [8]. The fracture toughness of these composites is comparable to those quoted for glass ceramics [15, 16], although far below the values reported for bone [25, 26].

As a first trial to assess bioactivity of the composites a very simple *in vitro* experiment was carried out, as described earlier. The surface of the HA-2 oxide composite was covered by a 2 μm thick apatite layer after 48 h immersion while only a few dispersed apatite crystals were found on the surface of HA, even after 7 days immersion, as may be seen in Fig. 4.

A common characteristic of bioactive ceramic materials is the formation of an apatite layer on their surface when immersed in simulated human blood fluid, as reported in the literature [27–29]. The formation of this layer on the surface of the material seems to be an essential requirement for bone bonding to occur [3, 5]. Although some doubts persist concerning the mechanism involved [27], the formation of this apatite layer seems to be related to the solubility of the bioactive materials [28, 30]. Both TCP and HA have been considered to induce the formation of this apatite

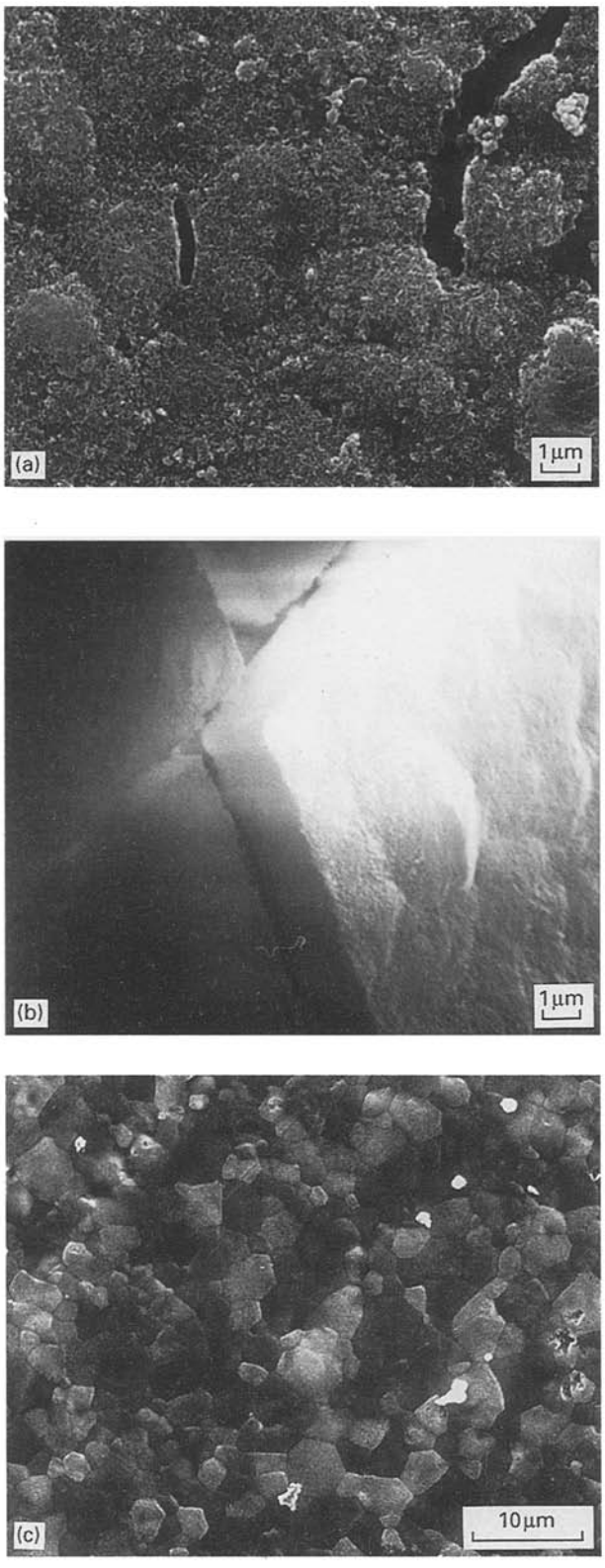

Figure 4 Apatite layer formed on the surface of HA–2 oxide composite after 48 h immersion: (a) cross-section showing an aproximately 2 μm thick layer; (b) on the HA control sample, only a few dispersed new apatite crystals were detected, even after 7 days immersion (c).

layer, but the former requires a shorter time to form the film [28]. The author made the assumption that this behaviour was related to the higher solubility of TCP.

The results obtained seem to be in good agreement with the above-stated principles, and therefore a higher apatite layer formation should be expected on the surface of these composites than on HA. We should also expect these materials to induce a faster bonding mechanism with bone. More complex *in vitro* studies and *in vivo* experiments using a rabbit model are currently under way to confirm the present results.

4. Conclusions

Phosphate-based glasses closely related to the chemical composition of the mineral part of bone can be incorporated in the microstructure of HA by a simple liquid phase process.

These composites have higher fracture toughness than sintered hydroxyapatite, most probably due to the high densification obtained, the smaller grain size and to the formation of TCP structures.

From the *in vitro* results we anticipate that the composites might show a higher rate of bone bonding leading to enhanced bioactivity. The faster formation of the *in vitro* apatite layer may be related to the presence of TCP in the microstructure of the composites.

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