JOURNAL OF Materials CHEMISTRY

Synthesis of biphasic ceramics of hydroxyapatite and β-tricalcium phosphate with controlled phase content and porosity

Xiaohong Yang[a] **and Zhihong Wang**[b]*

[a]*Department of Material Science, Lanzhou University, Lanzhou 730000, P.R. China*
[b]*Electronic Material Research Laboratory, Xi'an Jiaotong University, Xi'an 710049, P.R. China*

Received 16th March 1998, Accepted 1st July 1998

Biphasic porous ceramics of hydroxyapatite and β-tricalcium phosphate have been prepared. The process was based on solid state reactions of brushite with calcium carbonate. The optimum heat treatment conditions for producing pure stoichiometric HA, β-TCP and a biphasic composite of HA and β-TCP with definite phase composition were identified by the methods of thermal analysis, X-ray diffraction and IR absorption spectroscopy. As a gas-forming agent, a certain amount of uncalcined powder was mixed with the corresponding precalcined powder to produce porous ceramics with different microporosities. Foam ceramics with macropores have been prepared by a dipping technique. The pore structure was examined using scanning electron microscopy.

Hydroxyapatite (HA) and tricalcium phosphate (TCP), as two main calcium phosphate salts, have been studied extensively and used clinically. It is well known that the mineral constituent of human hard tissues generally shows a porous biphasic (HA + TCP) structure after being sintered at high temperature. Artificially sintered porous biphasic or multiphasic (HA + β- or α-TCP) bioceramics, which are analogous to bone mineral, are found to have better bone-bonding ability than pure HA in bony sites, and even show new bone formation within their porous structure in non-osseous tissues (a bone-inducing phenomenon). This phenomenon is mainly attributed to the excellent biodegradation of β-TCP.[1] Porosity control plays an important role in the design of this biphasic composite to promote both osteoconduction[2,3] and osteoinduction.[1] Accordingly, an implant with desired biodegradability can be obtained by controlling the content of β-TCP in a HA–β-TCP biphasic composite and the pore size of the implant. Therefore, many studies focus on the synthesis of these biphasic ceramics through various raw materials and processes, such as chemical coprecipitation from an aqueous solution of calcium nitrate and diammonium hydrogen phosphate,[4] and solid state reaction of tricalcium phosphate (TCP) with calcium hydroxide [$Ca(OH)_2$].[5]

The present study aims to prepare HA and β-TCP biphasic porous ceramics with controllable phase content and pore size which are suitable for biomedical applications.

Experimental

The synthesis process is based on two basic solid state reactions of brushite ($CaHPO_4\cdot 2H_2O$) with calcium carbonate ($CaCO_3$):

$$6CaHPO_4\cdot 2H_2O + 4CaCO_3 \rightarrow Ca_{10}(PO_4)_6(OH)_2(HA) + 14H_2O + 4CO_2$$

$$2CaHPO_4\cdot 2H_2O + CaCO_3 \rightarrow Ca_3(PO_4)_2(TCP) + 5H_2O + CO_2$$

Biphasic composites of HA and β-TCP with various phase compositions can be obtained by controlling the molar ratio of $CaHPO_4\cdot 2H_2O$ and $CaCO_3$ at an appropriate value between 1.5 and 2.0.

Moreover, $CaCO_3$ and $CaHPO_4\cdot 2H_2O$ themselves serve as pore-forming agents due to the evolution of carbon dioxide and water during the reaction, which leads to the development of a highly porous microstructure. It is possible to achieve porosity control by mixing various proportions of uncalcined and precalcined powders during sintering.

Appropriate molar ratios of brushite and calcium carbonate were mixed by ball-milling in ethanol for 22 h, using alumina media. The uncalcined raw materials were then obtained after drying the ball-milled slurry at 80 °C. The precalcining and sintering temperature depended on the composition of the biphasic composite and were determined by the results of thermal analysis (DuPont TA2000) and X-ray diffraction phase analysis (Rigaku D/Max 2400).

A dipping technique was employed to fabricate foam ceramics with large interconnected macropores. The ceramic slurry was prepared by ball milling the mixture of brushite and calcium carbonate with nominal composition in deionised water, and 1.5 wt.% PVA was added as an organic binder. Selected polymer foams with desired pore size were then dipped into the slurry so as to coat the skeleton of the foam with the calcium phosphate slurry. A porous ceramic with a replica of the network structure of the polymer foam was finally obtained by appropriate heat treatment. The pore structure was examined using scanning electron microscopy.

Results and discussion

Synthesis of pure hydroxyapatite

A $CaHPO_4\cdot 2H_2O:CaCO_3$ molar ratio of 1.5 is required to produce pure stoichiometric HA. Fig. 1–3 illustrate the results of thermal analysis for the raw material $CaHPO_4\cdot 2H_2O$, the uncalcined mixed powder and the powder precalcined at 1200 °C, respectively. Fig. 4 and 5 show the XRD patterns of the above raw materials under different heat treatment con-

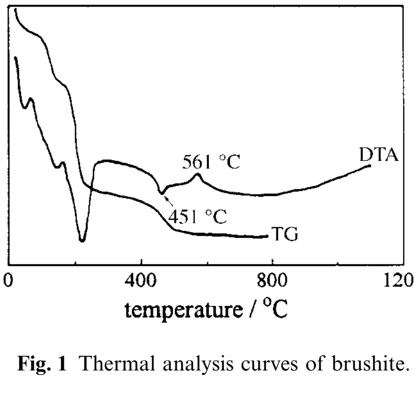

Fig. 1 Thermal analysis curves of brushite.

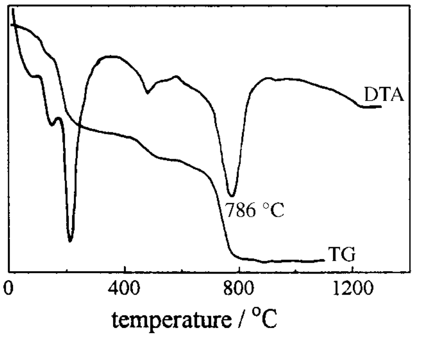

Fig. 2 Thermal analysis curves of uncalcined mixed powder of $CaHPO_4 \cdot 2H_2O$–$CaCO_3$ in a molar ratio of 1.5. The peak from 675 to 786 °C is the endothermal decomposition peak of $CaCO_3$.

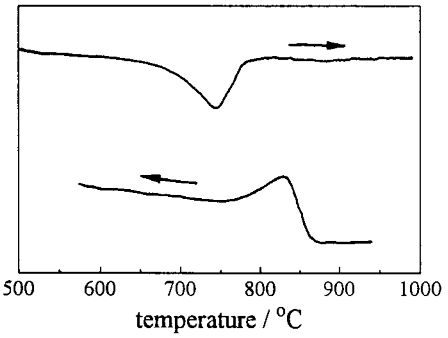

Fig. 3 DTA curves of pure hydroxyapatite.

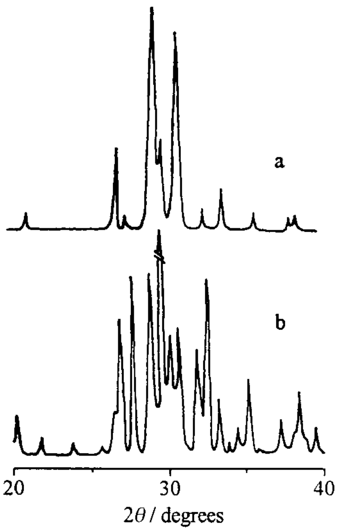

Fig. 4 X-Ray diffraction analysis of $CaHPO_4 \cdot 2H_2O$, after heat treatment at (a) 550 °C, γ-$Ca_2P_2O_7$ and (b) 800 °C, β-$Ca_2P_2O_7$.

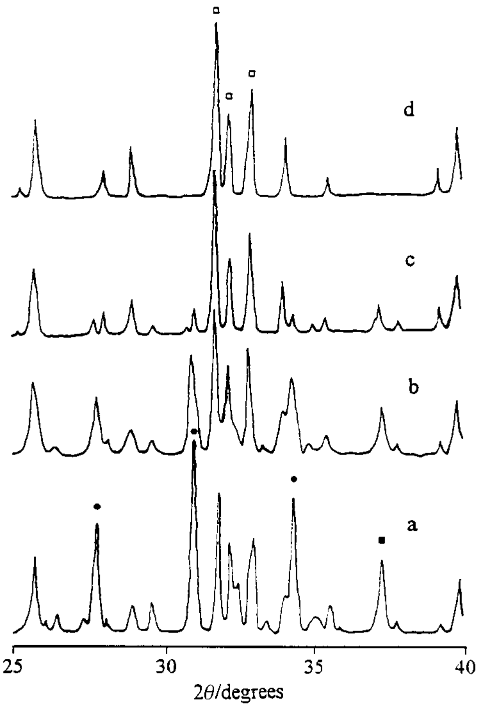

Fig. 5 XRD patterns of the starting materials of HA after calcination at (a) 1000 °C for 1 h, (b) 1000 °C for 4 h, (c) 1100 °C for 2 h, (d) 1200 °C for 2 h. (●) β-TCP, (□) HA, (■) CaO.

ditions. From Fig. 1 and 4, it can be concluded that the endothermal peak at about 451 °C on the DTA trace, accompanied by about 5% weight loss on the TG curve, is due to the loss of water from $CaHPO_4$ to form γ-$Ca_2P_2O_7$, and the exothermal peak at 561 °C is associated with the phase transition from γ-$Ca_2P_2O_7$ to β-$Ca_2P_2O_7$. In Fig. 2, the endothermal peak around 786 °C is due to the decomposition of $CaCO_3$. In Fig. 5, β-TCP is always observed below 1100 °C and the intensity of the main diffraction peak of β-TCP ($2\theta = 31°$) decreases with increasing calcination temperature and reaction time. This indicates that the formation of β-TCP is faster than that of HA, but HA is more thermodynamically stable than β-TCP. Hence, the formed β-TCP is continually reacting with CaO, which can also be detected below 1100 °C by X-ray diffraction, to form HA eventually. Fig. 5(d) shows the XRD pattern of pure hyroxyapatite. In Fig. 3, the endothermal peak during heating and the exothermal peak during cooling correspond to loss of water from pure HA and absorption of moisture by oxyapatite $Ca_{10}(PO_4)_6O$, respectively.

IR absorption spectra of the samples calcined at different temperatures for 2 h are shown in Fig. 6. The characteristic absorption band of OH^- at 632 cm^{-1} increased with increasing calcination temperature, while the absorption peaks[6] of $P_2O_7^{4-}$ at 553 cm^{-1} and 730 cm^{-1} disappeared when the calcination temperature was above 1100 °C. Accordingly, the optimum

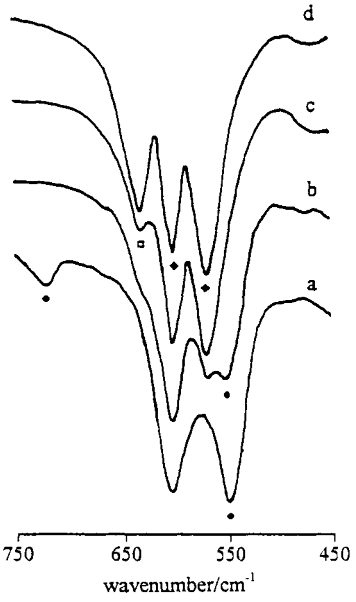

Fig. 6 IR absorption spectra of the starting materials of HA after calcination for 2 h at (a) 800 °C (b) 1000 °C (c) 1100 °C (d) 1200 °C. (●) $P_2O_7^{4-}$, (□) OH^-, (◆) PO_4^{3-}. With the formation of the stoichiometric HA, the shoulder at 632 cm^{-1} (OH^-) changes into a well defined peak coupled with the disappearance of the peaks of $P_2O_7^{4-}$ at 553 and 730 cm^{-1}.

heat treatment conditions for preparing pure hydroxyapatite are calcination at 1200 °C for 2 h.

Therefore, the detailed solid state reaction sequence between the starting powders upon heating can be concluded as follows:

$$6CaHPO_4{\cdot}2H_2O + 4CaCO_3 \xrightarrow{\sim 210\,^{\circ}C} 6CaHPO_4 + 4CaCO_3 + 12H_2O(g)$$

$$6CaHPO_4 + 4CaCO_3 \xrightarrow{450\text{–}470\,^{\circ}C} 3\gamma\text{-}Ca_2P_2O_7 + 3H_2O(g) + 4CaCO_3$$

$$3\gamma\text{-}Ca_2P_2O_7 + 4CaCO_3 \xrightarrow{\sim 563\,^{\circ}C} 3\beta\text{-}Ca_2P_2O_7 + 4CaCO_3$$

$$3\beta\text{-}Ca_2P_2O_7 + 4CaCO_3 \xrightarrow{670\text{–}786\,^{\circ}C} 3\beta\text{-}Ca_2P_2O_7 + 4CaO + 4CO_2(g)$$

$$3\beta\text{-}Ca_2P_2O_7 + 4CaO \xrightarrow{900\text{–}1100\,^{\circ}C} x\beta\text{-}Ca_3(PO_4)_2 + yCa_{10}(PO_4)_6O + mCaO + n\beta\text{-}Ca_2P_2O_7 \xrightarrow{\sim 1200\,^{\circ}C} Ca_{10}(PO_4)_6O$$

$$Ca_{10}(PO_4)_6O + H_2O \xrightarrow{\sim 850\,^{\circ}C} Ca_{10}(PO_4)_6(OH)_2$$

Synthesis of pure β-tricalcium phosphate

A $CaHPO_4{\cdot}2H_2O$:$CaCO_3$ molar ratio of 2 is required to prepare pure β-TCP. The thermal analysis results shown in Fig. 7 in conjunction with the X-ray diffraction patterns shown in Fig. 8 can suggest a detailed reaction scheme during heat treatment as follows:

$$2CaHPO_4{\cdot}2H_2O + CaCO_3 \xrightarrow{\sim 210\,^{\circ}C} 2CaHPO_4 + CaCO_3 + 4H_2O(g)$$

$$2CaHPO_4 + CaCO_3 \xrightarrow{450\text{–}470\,^{\circ}C} \gamma\text{-}Ca_2P_2O_7 + H_2O(g) + CaCO_3$$

$$\gamma\text{-}Ca_2P_2O_7 + CaCO_3 \xrightarrow{\sim 563\,^{\circ}C} \beta\text{-}Ca_2P_2O_7 + CaCO_3$$

$$\beta\text{-}Ca_2P_2O_7 + CaCO_3 \xrightarrow{\sim 765\,^{\circ}C} \beta\text{-}Ca_2P_2O_7 + CaO + CO_2(g)$$

$$\beta\text{-}Ca_2P_2O_7 + CaO \xrightarrow{\sim 920\,^{\circ}C} \beta\text{-}Ca_3(PO_4)_2$$

$$\beta\text{-}Ca_3(PO_4)_2 \xrightarrow{1000\text{–}1200\,^{\circ}C} x\beta\text{-}Ca_3(PO_4)_2 + y\alpha\text{-}Ca_3(PO_4)_2 + zCa_{10}(PO_4)_6O$$

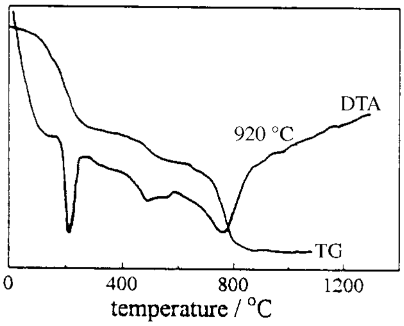

Fig. 7 Thermal analysis curves of uncalcined mixed powder of $CaHPO_4{\cdot}2H_2O$–$CaCO_3$ in a molar ratio of 2, the small peak at *ca.* 920 °C is an exothermal peak arising from the formation of β-TCP.

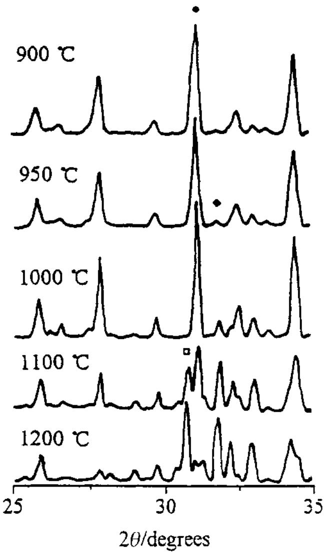

Fig. 8 XRD patterns of the β-TCP starting material fired for 2 h at different temperatures. HA starts to be present after firing at 950 °C. Above 1100 °C the HA phase content increases and the α-TCP phase is detected. (●) β-TCP, (□) α-TCP, (◆) HA.

It can be seen that the optimum heat treatment conditions for preparing pure β-TCP are sintering at 930 °C for 2 h. The HA and α-TCP phases will be present when the sintering temperature is above 950 and 1100 °C, respectively.

Synthesis of a biphasic composite of HA and β-TCP with controlled phase composition

As revealed above, the main problem of controlling the phase content of the biphasic composite is that the optimum calcination temperatures for β-TCP and HA are different. Hence, the key factor for control of the phase content is to select an appropriate sintering temperature. Since the phase transition temperature from β-TCP to α-TCP is above 1100 °C, the highest sintering temperature for ensuring a biphasic composite of HA and β-TCP *vs.* the formation of α-TCP is determined as 1100 °C. The phase contents are measured by the relative intensities ρ of the main diffraction peaks of HA ($2\theta = 31.8°$) and β-TCP ($2\theta = 31°$)

$$\rho = \frac{I_{HA}}{I_{HA} + I_{TCP}}$$

Mixtures of pure HA and pure β-TCP with various definite weight ratios were used as references to obtain a standard curve of relative intensity ρ *versus* HA weight content. The ball-milled starting materials of brushite and calcium carbonate were mixed according to a series of designed nominal compositions and then calcined for 4 h at either 1000 or 1100 °C. The relative intensities of the calcined powders were measured and

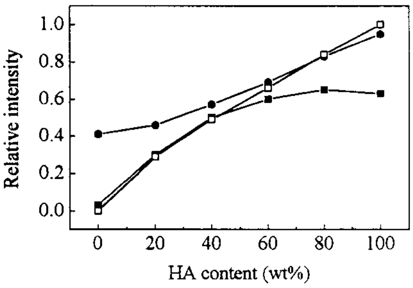

Fig. 9 Relative diffraction intensity *vs.* the weight content of the HA phase. The biphasic composites were sintered at 1000 °C (●) and 1100 °C (■), respectively. The standard curve (□) is also shown as a reference.

the results are summarized in Fig. 9. As shown in Fig. 9, the actual phase contents in the composites are consistent with the nominal composition only when they satisfy the following conditions. If the designed nominal composition has a larger β-TCP component, *i.e.*, more than 50% of the total content, the mixed powder should sinter at lower temperature, for example below 1000 °C, and if the composition has a larger HA content, the mixed powder should sinter at higher temperature, for example at 1100 °C. This means that in order to maintain the phase content of the composite at the required level, the sintering temperature must be adjusted according to its nominal composition.

Preparation of porous HA–β-TCP ceramics

As mentioned above, a porous microstructure is necessary for osteoconduction. In order to obtain porous ceramics with various HA and β-TCP phase contents, both an uncalcined mixture of $CaHPO_4 \cdot 2H_2O$ and $CaCO_3$ with a known phase composition, and the corresponding precalcined powder prepared by the method described above were employed as starting materials.

It should be possible to mix the two powders in various proportions to produce ceramics with various densities. The mixed powders were ground and uniaxially pressed at about 200 MPa. Disc samples were sintered for 8 h at temperatures ranging from 950–1100 °C according to the nominal compositions of the samples. Apparent porosities of the samples measured by the water immersion method are illustrated in Table 1. Apparent porosity is defined as the ratio of the open pore space of a specimen to its bulk volume, expressed as a percentage, and can be calculated by the formula

$$p_a = \frac{m_3 - m_1}{m_3 - m_2} \times 100\%$$

in which p_a is the apparent porosity, m_1 is the mass of the original fired specimen, m_2 is the mass of the specimen which is immersed in water, and m_3 is the mass of the water-saturated specimen.

It can be seen from Table 1 that the porosity increases with increasing HA content and decreases with increasing uncalcined powder content. The latter result may be associated with the different sintering reactivity of the two raw materials. The uncalcined powder has a superior sintering reactivity to that of the precalcined powder. Nevertheless, the degree of porosity in the pressed samples with different phase compositions could be controlled by adjusting the sintering conditions and the proportions of uncalcined and precalcined powders in the starting materials.

It has been revealed that porosity and pore size play an essential role in biomaterials design.[7–9] A minimum pore size of 100 μm is necessary for the porous implant materials to function well and a pore size greater than 200 μm is an essential requirement for osteoconduction.[3,8] An ideal cancellous bone graft substitute would mimic osteo-evacuated cancellous bone and have a thin lattice interconnected by pores of 500–600 μm.[9] It is obvious that the micropores in the uniaxially pressed bulk ceramic can not meet the requirement for the pore size of an implant. Thus, the design of porous implant materials with pore sizes larger than, for example, 200 μm, appears to be important for clinical applications. Accordingly, porous ceramics with the macropore structure mentioned above were fabricated by the dipping process.

Table 1 Apparent porosities of the pressed samples measured by the water immersion method

HA phase contents (wt.%)	Uncalcined powder proportions (wt.%)			
	0	25	75	100
20	33	29	24	23
40	32	26	31	26
60	35	36	32	30
80	36	42	35	31

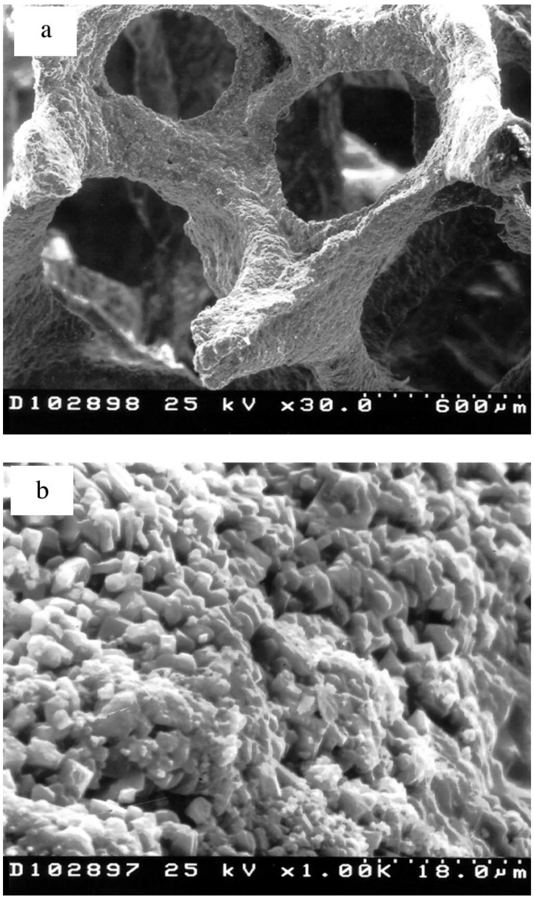

Fig. 10 SEM micrographs of biphasic foam ceramics sintered at 1100 °C for 2 h, consisting of 40 wt.% β-TCP and 60 wt.% HA; (a) macropores, (b) micropores.

Shown in Fig. 10 is a typical pore structure of the porous HA/β-TCP biphasic ceramic. It can be considered as an assembly of macroporosity and microporosity. The open-spaced foam structure is very similar to the idealized microstructure for cancellous bone regeneration described in ref. 9. The micropores can permit ingrowth of fibrovascular tissue and the large interconnected pores with sizes of 400–600 μm are necessary for differentiation of osteoblasts and opposition of new bone against this framework. The ingrowth of the fibrovascular tissue and the new bone can form a fibrous tissue reinforced composite and this is the so-called *in vivo* strengthening and toughening, which is an essential way to resolve the ultimate strength of a porous implant.

Conclusions

Pure, stoichiometric HA and β-TCP can be synthesized through the solid state reaction of $CaHPO_4 \cdot 2H_2O$ with $CaCO_3$ in molar ratios of 1.5 and 2. The optimum heat treatment conditions are sintering for 2 h at 1200 °C for HA and sintering for 2 h at 930 °C for β-TCP. Biphasic composites of HA and β-TCP with controlled phase compositions can be obtained by adjusting the sintering temperature from 1000–1100 °C. The composite with a higher HA nominal composition should sinter at higher temperature and *vice versa*. The biphasic foam ceramics with micropores and large interconnected pores, which resemble osteo-evacuated cancellous bone, can be fabricated by a dipping technique.

References

1 Y. Li and C. P. A. T. Klein, *J. Mater. Sci.: Mater. Med.*, 1994, **5**, 263.

2 I. H. Arita, V. M. Castano and D. S. Wilkinson, *J. Mater. Sci.: Mater. Med.*, 1995, **6**, 19.

3 D. Liu, *Ceram. Int.*, 1997, **23**, 135.

4 C. A. Tas, F. Korkusuz, M. Timucin and N. Akkas, *J. Mater. Sci.: Mater. Med.*, 1997, **8**, 91.

5 R. Rao, H. N. Roopa and T. S. Kannan, *J. Mater. Sci.: Mater. Med.*, 1997, **8**, 511.

6 R. A. Nyquist and R. O. Kagel, *Infrared spectra of inorganic compounds*, Academic Press, New York and London, 1971, p. 181.

7 E. W. White, *Mater. Res. Innovat.*, 1997, **1**, 57.

8 D. Muster, *Biomaterials—Hard tissue repair and replacement*, North-Holland, Amsterdam, 1992, p. 191.

9 E. C. Shors and R. E. Holmes, *Porous hydroxyapatite*, in *An Introduction to Bioceramics*, ed. L. L. Hench and J. Wilson, World Scientific Publishing Co., 1993, pp. 181–198.

Paper 8/02067A