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Resorbable, porous glass scaffolds by a salt sintering process

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Resorbable, porous glass scaffolds for tissue engineering were prepared by sintering borate glass with salt (sodium chloride). Subsequently, the sodium chloride was dissolved in water resulting in a highly porous material. By modifying the process parameters including salt particle size, salt volume percentage, sintering temperature and sintering time, sintered matrix structures were optimized. Analysis of the structure data indicates that the 50 vol% glass—50 vol% salt with particle sizes from 250–315 μm sintered at a temperature of 520°C for 10 min resulted in an optimum structure with 76.5% porosity and 29.3 N/cm^2 compressive strength. The process of HAP formation on the scaffolds in 0.25 M K_2HPO_4 solutions with pH 9.0 at 37°C was evaluated. The structural changes were analyzed by X-ray diffraction and scanning electron microscopy. An amorphous phosphate was formed on the surface of the scaffolds within 1d and crystalline hydroxyapatite (HA) within 10d.

1. Introduction

Nowadays, in modern medicine there is a growing approach to repair the bony tissue by using a porous scaffold that acts as a template for tissue regeneration [1–6]. In this trend, the development of different biodegradable, porous scaffolds plays an important part [7–10].

Since the discovery of Bioglass by Hench *et al.* [11, 12], various types of glasses and glass-ceramics have been investigated and some of them have been commercially used. Recently, researchers at the University of Missouri-Rolla have shown that some borate glasses can convert to hydroxyapatite and bond directly to bone in a manner comparable to the silicate-based 45S5 glass [13, 14]. However, little is known about the fabrication of the borate glasses into porous, three-dimensional scaffolds suitable for tissue engineering applications.

In this study, mixtures of a borate glass and salt (sodium chloride) particles of different size distributions were thermally heated. Subsequently, the salt was removed by dissolution in water and porous scaffolds were formed [15]. This method, the salt sintering method has previously been described in the literature for the preparation of highly porous phosphate glasses and glass-ceramics [16, 17] as well as for the preparation of glasses with large SiO_2 concentrations (>80%) [18]. In the present study, the method was applied to the preparation of highly porous borate glasses with large pore sizes. The effects of sintering process parameters including salt particle size, salt volume percentage, sintering temperature and sintering time on the structure were investigated. The bioactivity of the scaffolds was evaluated by the transformation of the scaffolds to hydroxyapatite in 0.25 M K_2HPO_4 solutions with pH 9.0 at 37°C. The effect of pore size on dissolving rate was studied and the surface morphologies, microstructures and chemical compositions were analysed.

2. Experimental procedure

A sodium calcium borate glass from the system $Na_2O{\cdot}CaO{\cdot}B_2O_3$ was melted at 1000°C, kept for 1 h in a platinum crucible. The glass was quenched, crushed and ground thoroughly. Using micron sieves, glass powders with particle sizes $\leq$20 μm were isolated. The glass powders were then thoroughly mixed with the salt (sodium chloride) with particle sizes of 0–160, 160–250, 250–315, >315 μm and various volume percentages.

Samples with the size 18 × 18 × 6–8 mm^3 were formed by pressing the mixed powders of glasses and sodium chloride. The samples were thermally treated at different temperature for 5 to 15 min and then immersed in water for 0–3 days to dissolve all the salt inside. Borate

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glass samples with different pore sizes and porosities were formed.

The evaluation of the sintered samples dealt with modification of sintering temperature and sintering time. The sintering temperature and time were chosen because it was thought that they would have direct effects on the structure and properties of the sintered matrix. Samples were prepared by sintering mixed powders at 480, 500, 520, 550°C for 5, 10 and 15 min. After dissolving the salt, the matrices were crushed and measured by DTA.

The average porosity of the samples was determined using the Achimedes' principle (e.g. described by Li [16]). In this method, ethanol with the density ρ_e was used as the displacement liquid. A density bottle filled with ethanol was weighted ($W1$). A sample weighted Ws was immersed into the density bottle and vacuum was attached in order to remove air from the pores of the material. Then the density bottle was supplemented with ethanol to full and weighted ($W2$). The sample which pores were now filled with ethanol was taken out of the density bottle and then the density bottle was weighted ($W3$). The porosity was calculated by the following formula:

$$\begin{aligned} \text{Volume of the sample pore}: Vp &= (W2 - W3 \\ &\quad - Ws)/\rho_e \\ \text{Volume of the sample skeleton}: Vs &= (W1 - W2 \\ &\quad - Ws)/\rho_e \\ \text{Porosity}: P = Vp/(Vp + Vs) &= (W2 - W3 \\ &\quad - Ws)/(W1 - W3 - 2Ws) \end{aligned}$$

The effect of calculated porosity on compressive strength was measured by Zwick 1446 testing machine. The surface morphologies of the samples were analysed by a Zeiss DSM 940A scanning electron microscope.

To evaluate the bioactivity of samples, the samples were immersed in 0.25 M potassium phosphate solutions with pH 9.0 at 37°C for up to 18 days. The surface morphology, microstructure and chemical composition were analysed by XRD and SEM. The surfaces were examined using a Zeiss DSM 940A scanning electron microscope using an accelerating voltage of 2 kV.

3. Results and discussion

XRD diffraction patterns of matrices sintered at 500, 520°C and 550°C for 10 min are shown in Fig. 1. After sintering at 550°C for 10 min, lines attributable to $Ca_2B_2O_5$ (JCPDS nr. 18-0279) and $CaNa_3B_5O_{10}$ (JCPDS nr. 37-0828) are observed. After thermal treatment at smaller temperatures, the samples are still amorphous. Structure optimisation was conducted by modifying salt particle size and induced salt volume as well as sintering temperature and time.

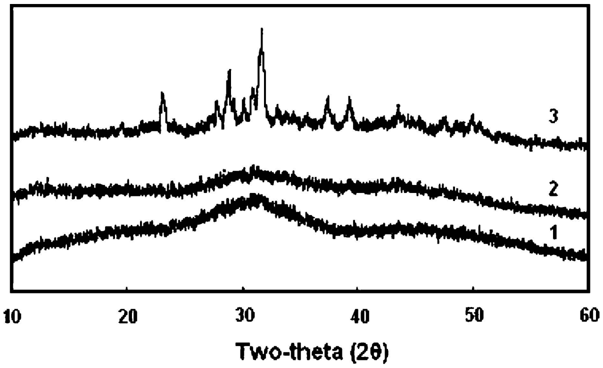


Figure 1 XRD patterns for samples sintered at 1. 500°C for 10 min, 2. 520°C for 10 min, 3. 550°C for 10 min.

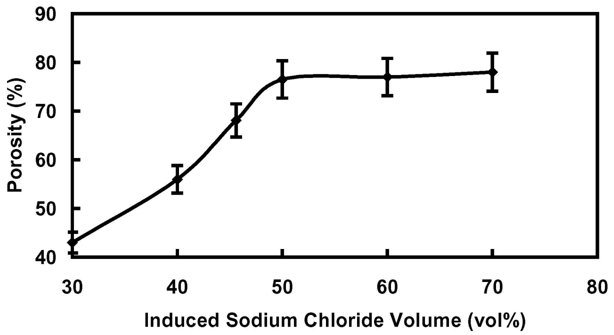


Figure 2 Porosity of 250–315 μm samples with different sodium chloride volume concentrations thermally treated at 520°C for 10 min.

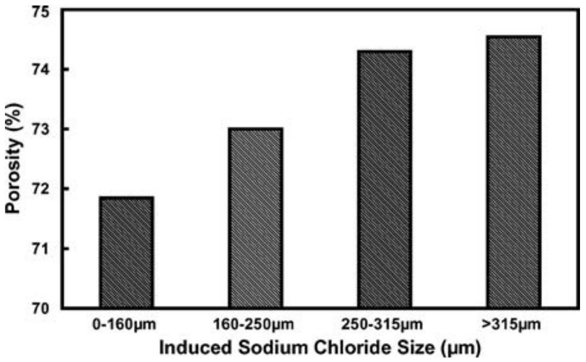
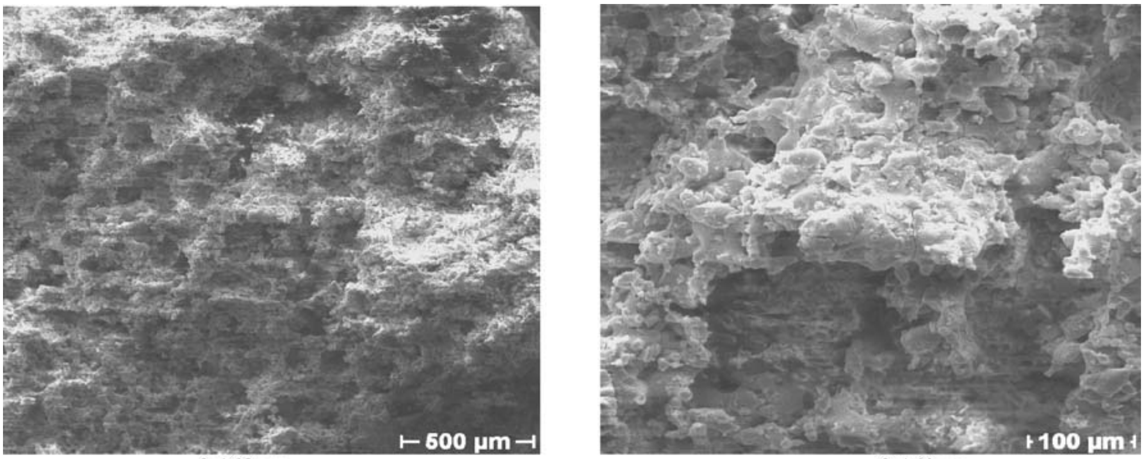
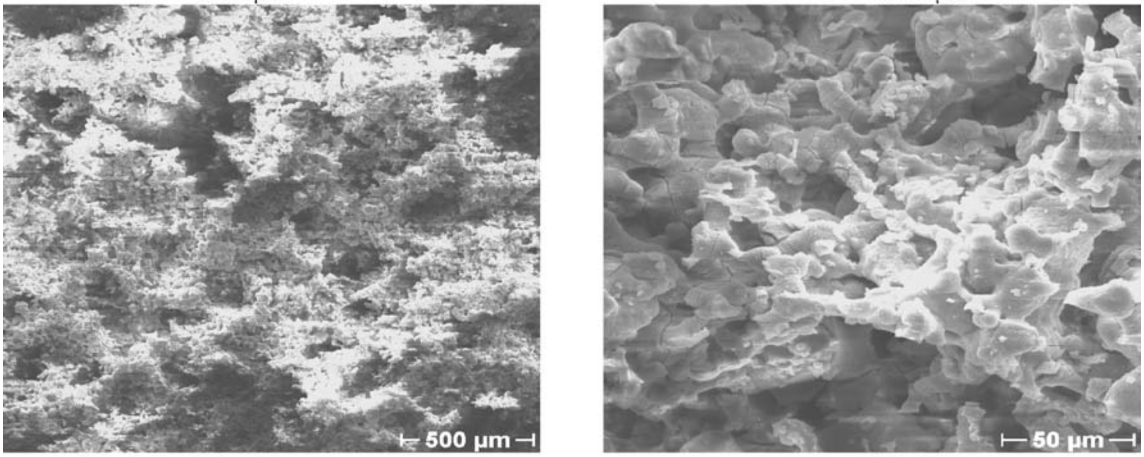


Figure 3 Porosity of 50/50 samples prepared using different sodium chloride particle sizes thermally treated at 520°C for 10 min.

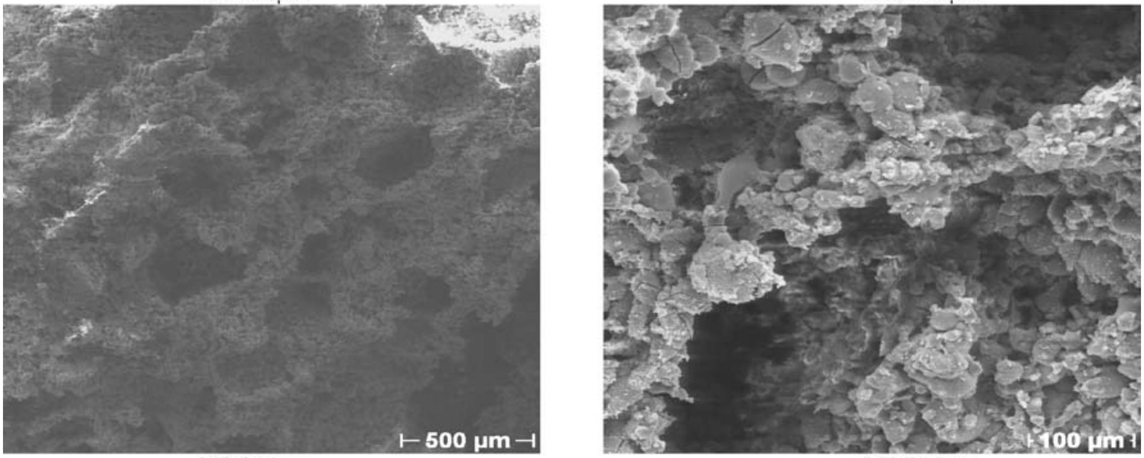
In order to find out suitable sintering temperature and time for mixed powders, samples were sintered at the temperature of 480, 500, 520, 550°C for 5, 10 and 15 min. It can be clearly seen that particles sintered at the temperature above or equal to 520°C for 10 min are bound together firmly enough. It is noticed that when the samples are sintered at 550°C, their colour changes from white to dark grey. Fig. 2 shows the porosity of samples thermally treated at a temperature of 520°C as a function of the volume concentration of the added sodium chloride. At 30 vol% NaCl, a porosity of 43% is obtained. With increasing the volume concentration of NaCl, the porosity of the thermally treated samples increases, at 50 vol% NaCl, a value of around 78% is reached. Further increasing the volume concentration of NaCl does not result in a further increase in porosity. The effect of the NaCl particle size on the porosity is shown in Fig. 3. It should be noted that in any case the measured porosity was larger than the volume percentage of NaCl. At a NaCl particle size fraction of 0–160 μm, the porosity is around 72%. Increasing the grain size results in a slight increase of the porosity. At NaCl grain sizes larger than 315 μm, a porosity of 74.5% is reached. The pore size and porosity are controlled by the particle size and the volume percentage of the salt, respectively. This salt sintering technique resulted in a semi-uniform three-dimensional structure as shown in Fig. 4. These micrographs show the typical structure of the porous matrix. The pores resulting from the leaching of NaCl can clearly be observed. Obviously, during thermal treatment, in any case interpenetrating microstructures consisting of the glassy phase and the NaCl phase were formed. The sample prepared using NaCl with grain sizes in the range from 250–315 μm exhibits the largest



0-160μm 0-160μm



160-250μm 160-250μm



250-315μm 250-315μm

Figure 4 SEM of 50/50 glass/salt samples prepared using different salt particle sizes, (i.e), pore size thermally treated at 520°C for 10 min.

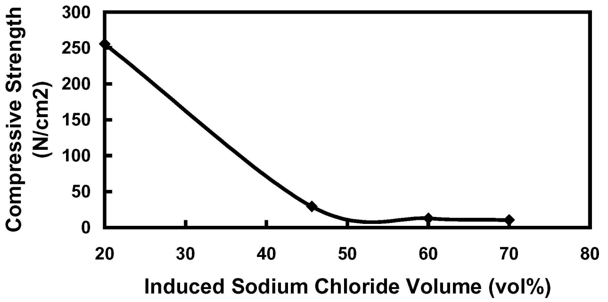


Figure 5 The effect of sodium chloride volume on compressive strength. Samples prepared using NaCl particles with grain sizes in the range from 250 to 315 μm sintered at 520°C for 10 min.

pores, that with grain sizes <160 μm the smallest pores. The large pores have a size approximately equivalent to the size of the NaCl grains used. In a higher magnification, it can be seen that the remaining phase insoluble in water is sintered, however, still exhibits microporosity. From the micrographs, an effect of NaCl particle size on porosity, can not be seen.

The effect of sodium chloride volume percentage on the compressive strength is shown in Fig. 5. At an NaCl volume concentration of 20%, thermal treatment at 520°C for 10 min resulted in a compressive strength of 250 N cm^{-2}. It can be seen that with increasing the volume concentration of sodium chloride, i.e., the porosity, the mechanical strength of the matrix after leaching decreases, which is easy to be understood.

Analysis of the structure data indicates that the 50 vol% glass—50 vol% 250–315 μm salt particles matrix sintered at a temperature of 520°C for 10 min resulted in an structure with 76.5% porosity and 29.3 N cm^{-2} compressive strength.

The weight loss of sintered and leached matrices, subsequently reacted in 0.25 M potassium phosphate solutions with pH 9.0 at 37°C is shown Fig. 6 as a function of the reaction time. The sample prepared using an NaCl grain size >315 μm had the highest weight loss rate. It experienced a relatively rapid weight loss within 10 d and only a small additional weight loss for larger times. The matrix sintered using sodium chloride with a particle size 0–160 μm had smaller weight losses and needed more time (12 d) to reach a constant value. After 12 h all studied samples reached, within the limits of error, a constant weight loss. The weight losses were approximately the same for all NaCl particles sizes and in the range from 66 to 69%. The theoretical weight loss (69%) was calculated by assuming all the Na_2O and B_2O_3 to dissolve completely while all the CaO has formed stoichiometric hydroxyapatite (HA). The measured weight loss is about 0 to 3% smaller than the theoretical value. This may be caused by deviations from stoichiometry of the formed HA (e.g., by the incorporation of carbonate or chloride in the lattice).

In order to further clarify the transformation process, the matrices prepared from salt with the pore size of 250–315 μm treated with the potasium phosphate solution for different periods of time were ground and XRD patterns were recorded (see Fig. 7). The XRD patterns of the matrix soaked in potassium phosphate for 1 d matrix did not show any hint at crystalline phases. XRD patterns of a samples soaked for 10 d in the potassium phosphate solution showed distinct lines all attributable to crystalline hydroxyapatite (JCPDS nr. 72-1243). The lines are notably broadened. Fig. 8 shows SEM micrographs of a glass sample prepared using 50 vol% NaCl with a grain size fraction of 250 to 315 μm before and after soaking 3 d in potassium phosphate solution. The pore sizes of the samples before soaking are in the 200 to 300 μm range. Additionally some micropores occur. After soaking in potassium phosphate solution, a fairly similar structure is observed. There are still large pores with sizes in the same range as in the unsoaked sample. In the micrographs with the higher magnification (see right), however, notable differences are observed. In the sample

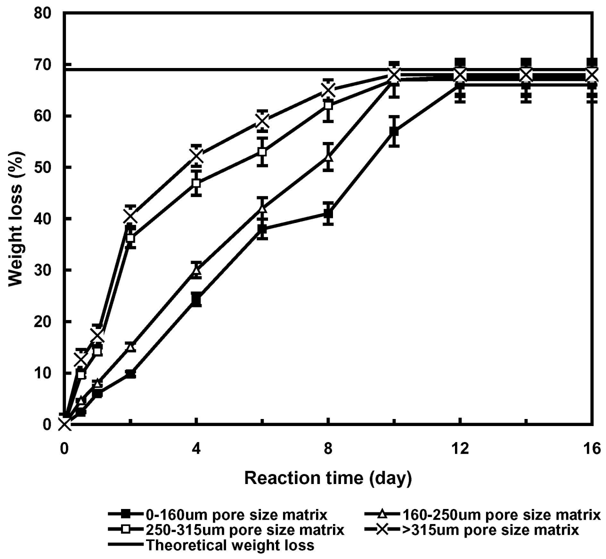


Figure 6 The weight losses of sintered samples (520°C, 10 min) with different pore sizes soaked in 0.25 M potassium phosphate solutions with pH 9.0 at 37°C.

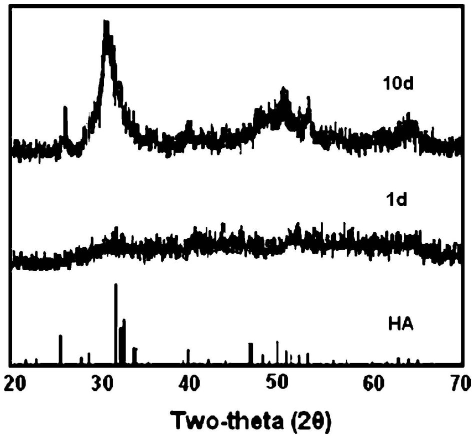
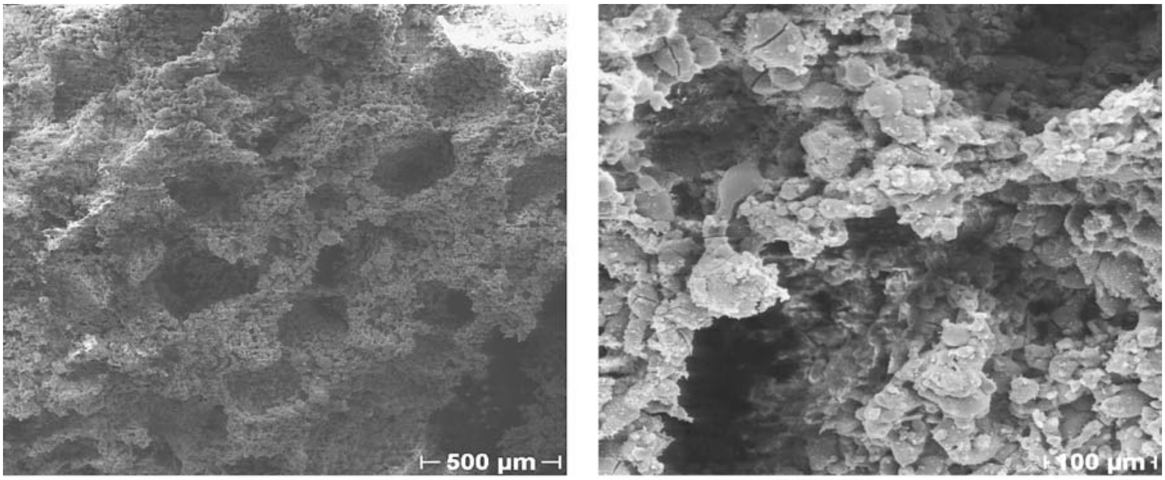
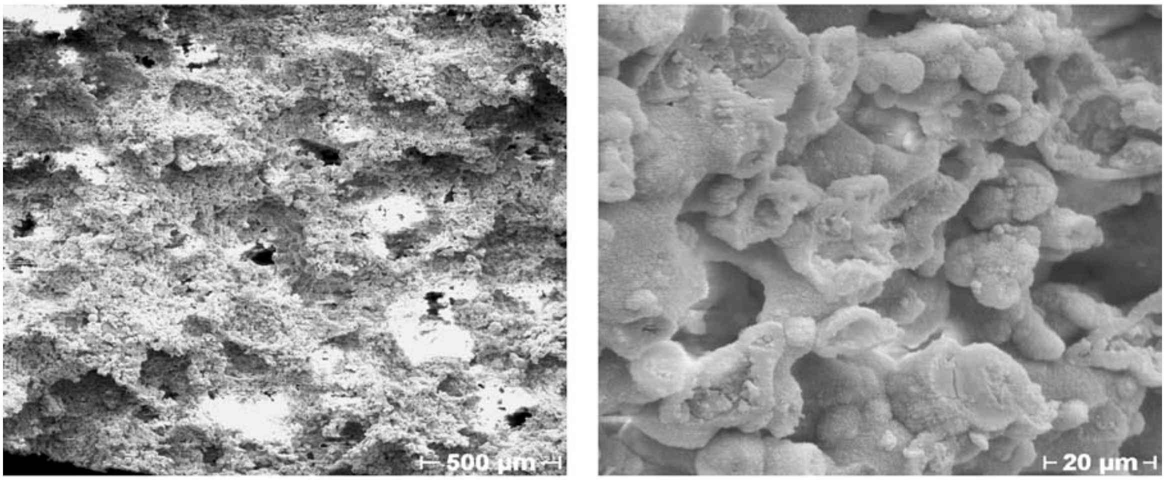


Figure 7 XRD patterns of samples soaked in 0.25 M K_2HPO_4 solutions for 1 d and 10 d.



Before reacted in 0.25M K_2HPO_4 solutions



After reacted in 0.25M K_2HPO_4 solutions

Figure 8 SEM micrographs of the 250–315 μm pore size samples before and after soaking in 0.25 M K_2HPO_4 solutions for 3d.

soaked in potassium phosphate solution, hydroxyapatite crystals are seen. The remaining micropores are notably smaller than in the unsoaked sample.

4. Conclusions

An $Na_2O/CAO/B_2O_3$ glass was powdered and mixed with sodium chloride particles with different particle sizes. Thermal treatment of the samples resulted in the formation of interpenetrating structures. The sodium chloride could be removed from the samples by dissolution in water. This resulted in highly porous structure formed by the borate glass. A sample with 50 vol% glass—50 vol% 250–315 μm salt particles sintered at a temperature of 520°C for 10 min possessed a structure with 76.5% porosity and 29.3 N cm^{-2} compressive strength. Borate glass scaffolds soaked in a 0.25 M K_2HPO_4 solution at 37°C and $pH = 9.0$ were converted into hydroxyapatite. This reaction increased steadily with time and was completed after approximately 10 days. The conversion reaction involved the initial formation of an amorphous calcium phosphate phase which later crystallised to hydroxyapatite. The weight loss of the samples observed during conversion in hydroxyapatite can quantitatively be explained assuming a dissolution of all Na_2O and B_2O_3 from the glass and a reaction of the CaO of the glass with the phosphate of the solution to hydroxyapatite.

Acknowledgments

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