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# Preparation of bioactive glasses with controllable degradation behavior and their bioactive characterization

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**Bioactive glasses and ceramics have been widely investigated for bone repair because of their excellent bioactive characteristics. However, these biomaterials undergo incomplete conversion into a bone-like material, which severely limits their biomedical application. In this paper, borosilicate bioactive glasses were prepared by traditional melting process. The results showed that borosilicate glasses possessed high biocompatibility and bioactivity. In addition, when immersed in a 0.02 mol/L K<sub>2</sub>HPO<sub>4</sub> solution, particles of a borate glass were fully converted to HA. The desirable conversion rate to HA may be achieved through the adjustment of the B<sub>2</sub>O<sub>3</sub>/SiO<sub>2</sub> ratio. The results of XRD and FTIR analysis indicated that the degradation product was carbonate-substituted hydroxyapatite, which was similar to the inorganic component of bone.**

borosilicate glass, bioactive glass, biodegradation, bioactivity

The repair of damaged bone tissue has been investigated widely for centuries. Tissue engineering developed in recent years has shown great potential for biological alternatives for implants<sup>[1]</sup>. For bone tissue engineering application, as a template of cell growth, scaffold materials provide the places for cell adhesion, proliferation and functionalization. Also, biomaterial scaffolds can guide the growth of new bone tissue and control the shape of new tissue. Therefore, the studies of scaffold materials have been an important part of bone tissue engineering<sup>[2]</sup>.

Both polymers and ceramics have been used currently as scaffold materials for bone tissue engineering<sup>[3–8]</sup>. Despite the fact that polymers are biodegradable *in vitro* and *in vivo*, these materials suffer from several shortcomings, such as poor wettability and biocompatibility, relatively low mechanical strength and potentially immunological reactions. Ca-P ceramics and bioactive glasses, such as hydroxyapatite (HA), tricalcium phosphate (TCP) ceramics, silicate-based bioactive glass

codenamed 45S5 (Bioglass<sup>®</sup>) and A/W glass-ceramics, have been widely used for healing bone defects. With amorphous structure, bioglass has higher bioactivity than Ca-P ceramics. Although these kinds of bioglass and glass-ceramics have excellent biocompatibility and produce few system toxicity or immunological reactions, they absorb slowly or undergo incomplete conversion into a bone-like material after *in vivo* implantation, which severely limits their biomedical application.

In this paper, novel borosilicate bioactive glasses with controllable degradation behavior were developed. This kind of glass possessed high biocompatibility and bioactivity. Compared with current bioglass, the most different point is that, when immersed in the phosphate solution, particles of a borate glass were generally dissolved, and eventually fully converted to HA. The desirable

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conversion rate to HA was achieved by replacing part of  $B_2O_3$  in borate glass with  $SiO_2$ . Our results suggested that the novel bioactive glass could avoid the shortcoming of incomplete degradation, and might be used as new scaffold materials for bone tissue engineering.

## 1 Experimental

Four types of glass samples (designated 0B, 1B, 2B and 3B, respectively) were prepared by melting reagent grade chemicals in a platinum crucible at 1100–1300 °C for 2 h, and the melts were poured between cold stainless steel plates. The resulting glasses were crushed and sieved to give particles with sizes in the range of 150–300  $\mu m$ . The compositions of these four glasses are given in Table 1.

**Table 1** The compositions of all four glasses (mol%)

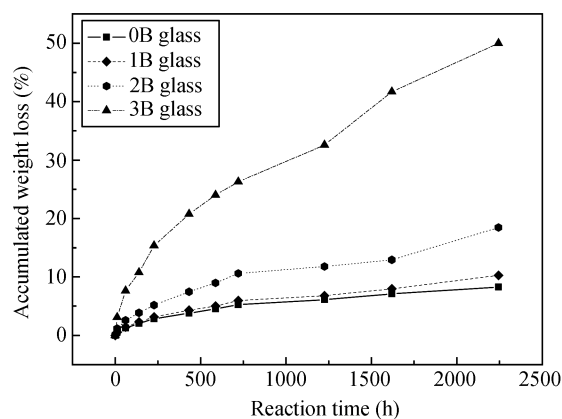
	$R_2O$	RO	$B_2O_3$	$P_2O_5$	$SiO_2$
0B glass	14	30	0	2	54
1B glass	14	30	18	2	36
2B glass	14	30	36	2	18
3B glass	14	30	54	2	0

In general, the *in vitro* bioactivity of biomaterial is evaluated by immersing it in SBF solution. The ionic concentration in SBF is  $Na^+$  142.0 mmol/L,  $K^+$  5.0 mmol/L,  $Mg^{2+}$  1.5 mmol/L,  $Ca^{2+}$  2.5 mmol/L,  $Cl^-$  148.8 mmol/L,  $HCO_3^-$  4.2 mmol/L and  $HPO_4^{2-}$  1.0 mmol/L<sup>[9]</sup>. Among them, only  $Ca^{2+}$  and  $HPO_4^{2-}$  have an important effect on the formation of HA. In this paper, to simplify and quicken the reaction of glass particles with the solution, 0.02 mol/L  $K_2HPO_4$  was chosen to ensure that sufficient  $PO_4^{3-}$  ions were available to react with all the  $Ca^{2+}$  of the glass to form HA.

For evaluation of the degradation, the glass samples were immersed in 0.02 mol/L  $K_2HPO_4$  at 37 °C for different immersing time up to 2244 h. After immersion, the samples were removed from the solution and weight losses were measured, and then the weight loss was plotted against immersion time. Formation of apatite-like layers on glass surfaces were determined by X-ray diffraction (XRD, Model D/max 2550v, Rigaku), Fourier transform infrared reflectance spectroscopy (FTIR, Model 1760-X, Perkin Elmer Corp., Norwalk, CT) and scanning electron microscopy (SEM, Hitachi S-4700).

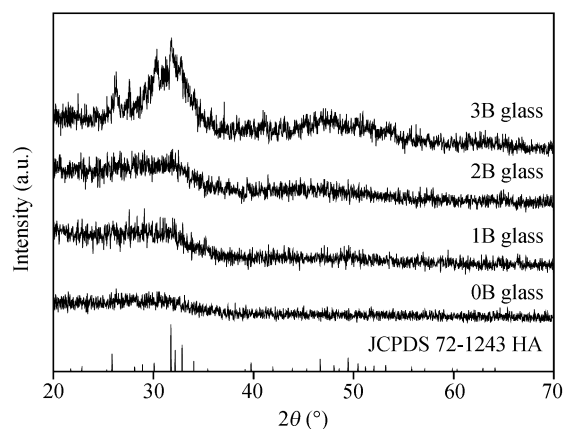
## 2 Results and discussion

Figure 1 shows the fraction weight loss versus reaction time of the four glasses during the immersion period. It can be seen that the maximum measured weight loss and dissolution rate increased with increasing  $B_2O_3/SiO_2$  ratio of the glasses. For borate glass (3B composition), the measured weight loss is >50% after 2244 h. After that, the slope of curve representing 3B glass has still a strong increasing tendency, indicating that the dissolutive reaction apparently continues until the weight loss reaches its theoretical maximum value at a certain time. With the continuity of the dissolution reaction, the glass would dissolve completely, and the alkaline earth ions could totally convert into HA and its solid solution. The remarkable discrepancy in the reaction rate among the glasses with different compositions is due to the difference in network structure. It is well known that the main structural units of the borate network are  $[BO_3]$  triangles and a small amount of  $[BO_4]$  tetrahedron<sup>[10]</sup>. Because of its three-fold coordination number, B cannot fully form three-dimension networks. The borate glass, therefore, has a lower chemical durability than that of silicate glass. The continuity and stability of the glass structure was improved when a part of  $B_2O_3$  in borate glass was replaced with  $SiO_2$ . As a result, the dissolution reaction slowed down. Therefore, the degradation behavior of borosilicate glass could be controlled by changing the compositions of the glass, namely, adjustment of the  $B_2O_3/SiO_2$  ratio, which consequently made the degradation speed matchable to the formation speed of bone tissue.



**Figure 1** Fraction weight loss versus reaction time of the four glasses during immersion in 0.02 mol/L  $K_2HPO_4$ .

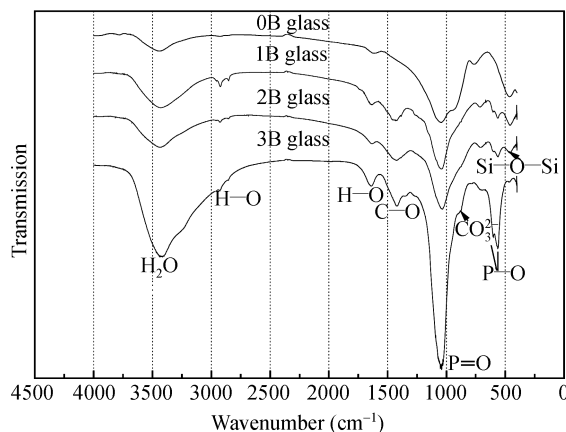
XRD patterns of the four glasses after immersed in 0.02 mol/L  $K_2HPO_4$  for 2244 h are shown in Figure 2. The spectrum of pure HA is also shown for comparison purposes. The major peaks in the patterns corresponded to those of a standard HA,  $Ca_{10}(PO_4)_6(OH)_2$  (JCPDS 72-1243), indicating the formation of HA during the reaction for all the four glass samples. Moreover, with increasing the  $B_2O_3/SiO_2$  molar ratio, the intensity increase of a maximum, corresponding to the (211) HA reflection, was observed in the XRD patterns, suggesting that the borate glass possesses stronger ability to induce HA than that of silicate glass. For all cases, it is clear that the diffraction peaks of the reacted glasses are broader and less intense. Especially, the diffraction peaks at  $2\theta = 25.8^\circ$  (102),  $29.1^\circ$  (210),  $31.9^\circ$  (211),  $32.3^\circ$  (112),  $32.7^\circ$  (300) and  $34.1^\circ$  (202) are so broad that all the peaks in the range of  $28-34^\circ$  form one broad diffraction peak. The broadening may be indication that the as-formed HA was poorly crystallized or that the crystallite size of the HA was on a nanometer scale, or a combination of both.



**Figure 2** XRD patterns of the four glasses after being immersed in 0.02 mol/L  $K_2HPO_4$  for 2244 h.

Figure 3 shows the FTIR spectra of the four glasses after immersing in 0.02 mol/L  $K_2HPO_4$  for 2244 h. The bands at  $560$  and  $605\text{ cm}^{-1}$ , corresponding to P—O symmetric stretching vibration in  $PO_4^{3-}$  groups in the HA lattice<sup>[11]</sup>, was observed for all four glasses, providing further indication for the formation of a HA layer on the surface of the glasses immersed in 0.02 mol/L  $K_2HPO_4$ . The bands at  $1415$  and  $866\text{ cm}^{-1}$  were attributed to the C—O resonance in  $CO_3^{2-}$  function group<sup>[12]</sup>. Since the present experiments were carried out in air, it is likely

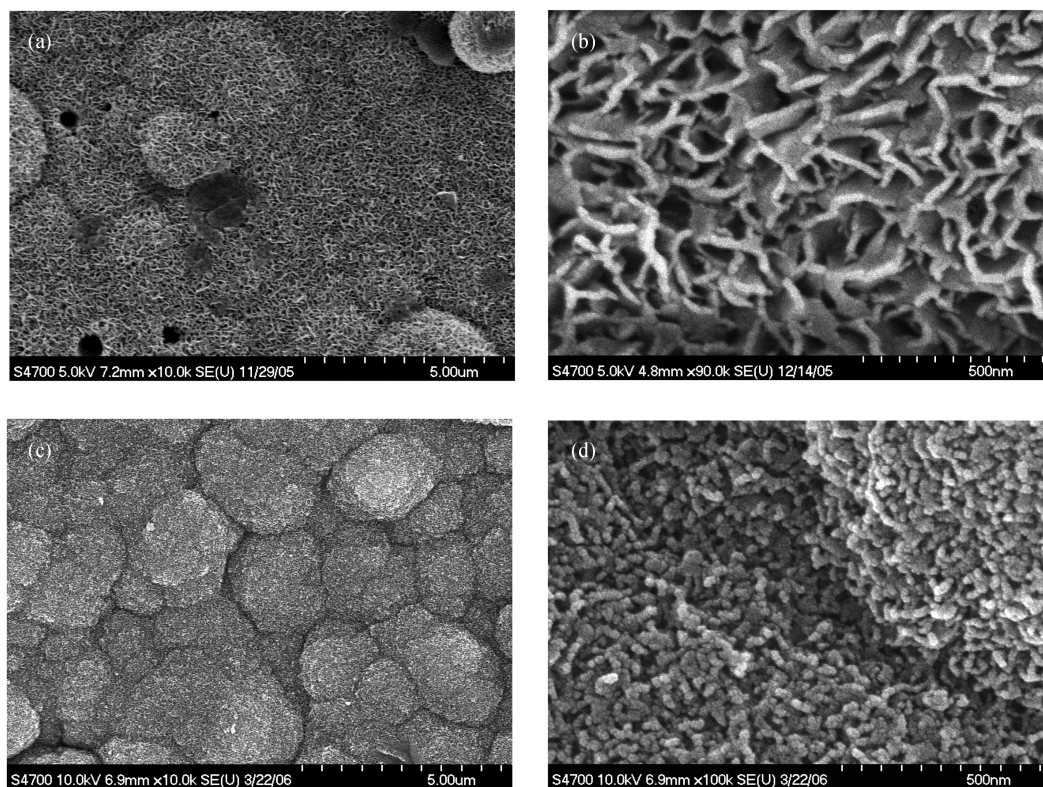
that  $CO_2$  from the atmosphere dissolved into the solution, reacting with HA to *in situ* form carbonate-substituted HA. The FTIR spectra in Figure 3 also show a resonance at  $440\text{ cm}^{-1}$  for the products of 0B, 1B and 2B glasses but not for the 3B glass. It was attributed to the Si—O—Si bending vibration in  $SiO_4^{4-}$  group<sup>[12]</sup>, suggesting that 0B, 1B and 2B glasses were only partially converted to HA and residual  $SiO_2$  or unconverted soluble  $SiO_2$ -rich gel layer was left in the reaction products<sup>[13]</sup>.



**Figure 3** FTIR spectra of the four glasses after being immersed in 0.02 mol/L  $K_2HPO_4$  for 2244 h.

Figure 4 shows the SEM micrographs of the 0B and 3B glasses after immersed in the phosphate solution for 2244 h. After immersion, the 0B and 3B glass surfaces were fully covered by HA layers. High-resolution SEM (Figure 4(b)) showed that the as-formed HA layer was highly porous on the 0B glass surface. On the 3B glass surface (Figure 4(d)), however, the HA layer was denser and consisted of numerous worm-like crystals with the diameter of 20 nm and length varying from 50 to 100 nm.

The formation of a HA layer *in vitro* is indicative of a biomaterial's ability to induce the HA layer<sup>[14]</sup>. With the continuity of conversion reaction, the precipitated HA reacts with  $CO_2$  from the atmosphere dissolved into the solution, forming *in situ* carbonate-substituted HA, which was similar to the inorganic component of bone. It has been proven that the material is bioactive if it can react with SBF solution to form HA<sup>[15]</sup>. Our results suggest that the as-prepared borosilicate glass have the ability to induce HA formation on their surfaces when immersed in the phosphate solution, which confirms the bioactive character of the novel glass. In addition, the



**Figure 4** SEM micrographs of 0B (a, b) and 3B (c, d) glasses after being immersed in 0.02 mol/L  $K_2HPO_4$  for 2244 h.

formation of a HA layer on the borate glass (3B) is faster than that on the silicate glass (0B). It is therefore believed that borate glass and borosilicate glass possess higher bioactivity than silicate glass.

The conversion of borosilicate glasses to HA is believed to follow a set of dissolution-precipitation reactions. As mentioned above, borosilicate glasses possess high chemical activity because of the structural characteristics of the glasses. When the glasses immersed in the phosphate solution, the B—O network structure of the glass is attacked by the solution at the same time, alkali and alkaline earth ions dissolved from the glass into the solution. Immediately, the  $PO_4^{3-}$  ions from the solution react with alkaline earth ions located on the glass surface, leading to nucleation of HA<sup>[16]</sup>. The precipitated HA is highly porous, providing for easy ionic transport through it. The continuation of the dissolution-precipitation reactions leads to thickening of the HA layer from the surface of glass particle inward, and eventually converting *in situ* to stable HA crystal.

### 3 Conclusion

Novel borosilicate bioactive glasses have been prepared by traditional melting process. The study on *in vitro* biodegradation and bioactivity showed that these glasses underwent incomplete conversion into a bone-like material in the phosphate solution. The desirable conversion rate to HA may be achieved through the adjustment of the  $B_2O_3/SiO_2$  ratio. Moreover, the degradation product was carbonate-substituted hydroxyapatite, which was similar to the inorganic component of bone. Therefore, the novel bioactive glass could avoid the shortcoming of incomplete degradation, and might be used as new scaffold materials for bone repair and bone tissue engineering.

Currently, the preparation of porous borosilicate bioglass scaffolds and the study on the biodegradation and bioactivity of these glass scaffolds are under way. Additionally, the degradation mechanism and the effect of degradation products on cell adhesion, proliferation and differentiation will also be studied.

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