FULL PAPER

Structure, degradation and hydroxyapatite conversion of B-doped 58S bioglass and glass-ceramics

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Bioglass has been widely applied in biological tissue engineering and other medical fields for many years. However, there are still many shortcomings in the application of bioglass, which needs further research. In this article, boron doped bioglasses were synthesized and characterized to evaluate the influence of the presence of B on degradation performance and biological activity. All sieved particles are irregular particles of micro-nano scale. After heat treatment at 600°C, the samples were amorphous, while microcrystals were produced in the sample heat treated at 800°C. X-ray diffraction and Fourier Transform Infrared Spectroscopy analyses indicate that the incorporation of boron changes the glass grid structure and promotes the formation of calcium silicate crystals in the case of heat treatment at 800°C. A dissolution study in simulated body fluid (SBF) was carried out, and ion release profiles and hydroxylapatite formation of the bioglasses were assessed. The test results show that the doping of B promotes the degradation of the samples, and the release of the Si in SBF influence the formation of the hydroxyapatite. And CaSiO₃ crystals in the samples heated at 800°C could release silicon quickly, which improve the bioactivity of bioglass-ceramics. In brief, the incorporation of B promotes the biodegradation and bioactivity of bioglass and bioglass-ceramics, and enhances bioglass performance, and thus, they are promising candidates for bone tissue engineering.

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1. Introduction

Tissue engineering seeks to promote the regeneration ability of host tissue through a designed scaffold that is populated with cells and signaling molecules.^{1)–3)} Various materials such as polymers and ceramics have been used as scaffold biomaterials in tissue engineering research.⁴⁾ But the all early biomaterials were applied to replace diseased, damaged or aging tissues, and those materials called “bioinert” should match the physical properties of the replaced parts.^{5),6)}

In 1969, a new material called bioactive glasses (BGs or bioglass) was invented by Hench, Splinter, et. al at the University of Florida, and it is considered as the third generation biomaterials used in bone tissue engineering for tissue regeneration due to its excellent biocompatibility and the ability of bone bonding.^{2),5),7),8)} The bone-bonding behavior has been associated with the formation of a carbonated hydroxyapatite (HA) layer on the bioglass surface through the interfacial reaction with biological fluids, and the layer could allow the chemical bond to host tissue, and the stages were reported by Hench.^{9)–12)} In the environment of body fluid or simulated body fluid, ions in bioglass, such as Ca²⁺ and Na⁺, exchange rapidly with H⁺

or H₃O⁺ from solution, which causes the breaking of Si–O bond on the glass surface and Si⁴⁺ ions are separated from the bioglass network into the solution.^{13),14)} At the same time, a Si–OH gel layer forms on the scaffolds surface, and the Si-rich layer promotes the migration of Ca²⁺ and PO₄^{3–} groups and the formation of a CaO–P₂O₅-rich film on the top of Si-rich layer. Then the amorphous Ca–P layer transforms to a mixed HA layer through incorporation of OH[–], CO₃^{2–} or F[–] anions from body fluid.¹⁴⁾

As a biomaterial, bioglass should at least have the following characteristics: (1) controllable biocompatibility and resorption rate;^{15),16)} (2) suitable surface chemistry for cell attachment and proliferation;¹⁶⁾ (3) excellent mechanical properties.¹⁶⁾ To match those requirements and improve the performance of existing biomaterials, researchers have done substantial work on the composition and preparation process of biological materials and have made great progress.^{17)–19)} The original bioglass was prepared by high-temperature melting method, and the material obtained by this method has high density and certain requirements for the ratio of materials. Subsequent generations of bioglass relied on sol–gel method which allows for bioactive glass production even with a greater addition of SiO₂, which is not always feasible using high-temperature methods.^{20)–22)} In addition to sol–gel method, changes in materials composition can also control the material performance, and

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borate BGs have been shown to support cell growth, adhesion, differentiation, and inducing neovascularization of newly formed tissues.^{23),24)} It was also reported that boron doping could modify the lattice structure of the bioglass, and the crystallites in the glass also affects the material performance and increases the biodegradation rate.

The objective of this article is to explore the B-doping effect on the bioglass materials on the glass structure, microcrystalline structure of silicate glass, and even the degradation performance, providing a research basis for the application and further development of materials.

2. Experimental

2.1 Synthesis of the samples

The composition of all investigated BGs in this work is shown in **Table 1**, named 58S, 58S-B-1, 58S-B-2, 58S-B-3, 58S-B-4. The acid-catalyzed sol-gel protocol was used to synthesize BGs, and this method consists of six stages: mixing, casting, aging, drying, and stabilization.²⁵⁾ A quantity of tetraethyl orthosilicate, 2M nitric acid, triethyl phosphate, Ca (NO₃)₂ and H₃BO₃ were added into the deionized water in sequence, and then a transparent sol was obtained by stirring the reaction mixture.

The resultant sol was placed at room temperature for 3 days to allow hydrolysis and poly-condensation. The gel then was dried for 24 h at 80°C, and then 120°C for 24 h. After drying, the white BGs powder was obtained. Finally, the white BGs powder was heat treated at 600 and 800°C in a muffle furnace for 3 h. Calcined samples obtained were named 58S-B-X-600°C and 58S-B-X-800°C.

2.2 Physicochemical characterization studies

X-ray diffraction (XRD), Fourier Transform Infrared Spectroscopy (FTIR), and a scanning electron microscope were used to analyze the physicochemical characterization of the samples. XRD (XRD-6000-Japan) was used to detect the possible presence of phases. Functional groups in BG materials were tested with FTIR (VERTEX 70-German). The surface morphology of the particles was investigated by a scanning electron microscope (SEM).

2.3 SBF dissolution

Simulated body fluid (SBF) was prepared according to the method of Kokubo.²⁶⁾ To make 1000 mL of SBF, the following reagents were dissolved in 800 mL of deionized water in order:²⁷⁾ 7.9960 g of NaCl, 0.3500 g of NaHCO₃, 0.2240 g of KCl, 0.3026 g of K₂HPO₄·3H₂O, 0.3255 g of MgCl₂·6H₂O, 20 ml of 2 M hydrochloric acid (HCl),

0.2780 g of CaCl₂, 0.0710 g of Na₂SO₄, 6.057 g of TRIS (hydroxymethyl) amino methane [(CH₂OH)₃CNH₂]. Then the bottle was filled to 1000 mL with deionized water, using 1M hydrochloric acid to adjust the pH of the SBF to 7.3.

2.4 In vitro bioactivity tests

The degradation and HA conversion of B-doped 58S bioglass were studied using the standard in vitro procedure described by Kokubo.^{1),26)} 40 mg of every BG powder after heat treatment, 58S-B-X-600°C and 58S-B-X-800°C, was immersed in 20 mL SBF, and placed in a shaking incubator at 37°C and 120 rpm. A quantity of 2 mL of SBF supernatant was taken for ICP-OES analysis at each time point (24, 72, 120, 360 h), and then 2 mL fresh SBF was added to keep the the sample powder-SBF ratio of 2 mg/mL. 1 M HCl was used to adjust the pH of the SBF to around 7.3, which is close to the pH of human body. The pH of each sample was measured at each time point by a pH pen with oakton general-purpose glass pH probe. Finally, the SEM, FTIR and XRD were used to evaluate the samples after immersing in SBF.

3. Results and discussion

3.1 Preparation of BGC nanoparticle

The powder materials prepared by the sol-gel method were all amorphous materials. After heat treatment, the organic components produced during the preparation were thermally decomposed, and the glass lattice structure of the bioglass also changed. It can be demonstrated by the XRD analysis. XRD patterns of the samples before immersion in SBF are shown in **Fig. 1**. Figure 1(a) displayed the XRD patterns of the BGs calcined at 600°C. One broad peak can be seen at 30°, but there is no existence of distinct peaks indicating the presence of a crystalline phase. All BGs after heat treatment at 600°C had XRD patterns of an amorphous state, while other samples heat-treated at 800°C before immersion indicated a presence of crystals. Figure 1(b) shows the XRD patterns of samples calcined at 800°C, and the XRD pattern shows the crystalline characteristics of HA and CaSiO₃. Diffraction peaks are revealed at 25.7, 31.78 and 32.19° corresponding to the (002), (211), (112) reflection of HA phase,^{28),29)} and this kind of peaks are presented in all samples at the sintering condition of 800°C. The 58S-800°C contained only HA crystallites, while CaSiO₃ existed in other 800°C heat-treated samples. This indicated that the incorporation of boron promoted the formation of crystallites. All the results above demonstrate that the increase of boron improves crystallization process but B does not enter in the crystallites.

The intermolecular interaction of the particles was determined by FTIR analysis (**Fig. 2**). **Table 2** is a comprehensive list of the optical vibrations referring to different functional groups in gel-derived B-doped glass-ceramic before and after immersion in SBF. The strong absorption band at 470 cm⁻¹ was caused by the vibration of the Si-O-Si symmetric bending,³⁰⁾ and the peak at 800 cm⁻¹

Table 1. Composition of B-doped bioglass samples

Sample ID	Reactants (Mole %)			
	SiO ₂	P ₂ O ₅	CaO	B ₂ O ₃
58S	60	4	36	0
58S-B-1	55	4	36	5
58S-B-2	50	4	36	10
58S-B-3	45	4	36	15
58S-B-4	40	4	36	20

Fig. 1. XRD patterns of the samples before immersion in SBF (a) samples sintered at 600°C for 3 h, (b) samples sintered at 800°C for 3 h.

Fig. 2. FTIR of the samples before immersion in SBF (a) samples sintered at 600°C for 3 h, (b) samples sintered at 800°C for 3 h.

Table 2. Comprehensive list of the optical vibrations referring to different functional groups in gel-derived B-doped glass-ceramic before and after immersion in SBF

Wavenumber (cm ⁻¹)	Assignment
440–460	the Si–O–Si symmetric bending ³⁰⁾
570	P–O asymmetric bending (HA) ³³⁾
606	P–O asymmetric bending (HA) ³³⁾
800	Network structure of SiO ₂ glass; Si–O–Si stretching between tetrahedral ^{31),32)}
960	Si–OH symmetric stretching ³³⁾
1000	SiO ₄ tetrahedra stretching ³¹⁾
1040	P–O stretching vibrational mode of PO ₄ ³⁻ tetrahedral from HA ^{28),30)}
1000–1100	P–O stretching in the glass network, ³⁵⁾ non-bridging oxygen atoms in the Si–O–Si bond, ^{28),35)} Si–O–Si stretching ^{31),43)}
1100	Asymmetric stretching vibration of B–O bonds from BO ₄ units ³⁴⁾
1170	Si–O–Si stretching in the glass network ³⁵⁾
1200–1400	B–O stretching vibration in BO ₃ units ^{34),36)–38)}
1600	bending vibration modes of O–H groups ^{39),40)}
3400	bending vibration modes of O–H groups ^{39),40)}

indicates the network structure of SiO_2 glass and Si–O–Si stretching between tetrahedrals.^{31),32)} The broad-band in the range $900\text{--}1250\text{ cm}^{-1}$ contains complex absorption peaks of multiple groups, such as Si–OH symmetric stretching,³³⁾ P–O stretching vibrational mode of PO_4^{3-} tetrahedral from HA, and asymmetric stretching vibration of B–O bonds from $[\text{BO}_4]$ units.^{30),34)} In addition, the shoulder at 1060 cm^{-1} was caused by the vibration of two non-bridging oxygen atoms in the Si–O–Si bond,^{28),35)} while the peaks around 1170 and 1045 cm^{-1} are assigned to Si–O–Si and P–O stretching in the glass network.³⁵⁾ Another band at $1200\text{--}1400\text{ cm}^{-1}$ is the main feature of B–O stretching of trigonal $[\text{BO}_3]$ units,^{34),36)–38)} and a doublet corresponding to the bending vibration modes of O–H groups is observed at 1640 and 3496 cm^{-1} .^{39),40)} The double bands at 570 and 602 cm^{-1} were caused by the P–O asymmetric bending in PO_4^{3-} group,³³⁾ and another weak peak around 1040 cm^{-1} is identified as P–O stretching vibrational mode of PO_4^{3-} tetrahedral from HA.^{28),30)}

As seen in Fig. 2(a), the peak at about 1400 cm^{-1} representing the structure of $[\text{BO}_3]$ became stronger with the increase of boron content, which indicates an increase of $[\text{BO}_3]$ in the glass. The peak also moved towards the low wave number direction gradually as a result of the increase of $[\text{BO}_4]$. This is because $[\text{BO}_3]$ and $[\text{BO}_4]$ in the glass are connected to each other but their B–O bond strength is different. With the increase of boron content, ever-increasing $[\text{BO}_4]$ caused the peak at 1400 cm^{-1} to shift towards the low wave number direction. The band between 900 and 1200 cm^{-1} includes many characteristic peaks of the group seen commonly in the glass structure, and it can be compared with the data after soaking to analyze the change of the glass structure. There are some new peaks in Fig. 2(b), such as 570 , 606 and 1040 cm^{-1} , that illustrate the appearance of HA in samples heated at 800°C . Two obvious different peak from Fig. 2(a) are the peak at 1400 cm^{-1} and the peak at 1100 cm^{-1} . The peak at 1400 cm^{-1} is lower than the one in Fig. 2(a), while the peak at 1100 cm^{-1} is greater than the one in Fig. 2(a). This indicates more B entered in

to the $[\text{BO}_4]$ structure in the case of heat treatment at 800°C . In addition, other bands representing different Si–O band also changed, and it shows the change of the glass grid structure with increased siloxane tetrahedron.

3.2 In vitro dissolution study

After 15 days of immersion in SBF, the cumulative ion release of boron and silicon in SBF from the powder samples was measured by ICP-OES, as shown in Figs. 3 and 4. Figure 3 shows the content of Si and B in the culture medium of 600°C sintered bioglass samples. As we can see in Fig. 3(a), the concentration of B in SBF increased sharply until 120 h , and then went up slightly. The data in Fig. 3(b) is the content of Si in culture solution, which indicates that all samples released Si rapidly at the very beginning, and $58\text{S-}600^\circ\text{C}$ had a maximum release before 24 h due to the maximum silicon content in the solid sample. But the Si concentration of $58\text{S-}600^\circ\text{C}$ changed slightly after 24 h . As for other four samples, the Si content in the solution increased steadily after 24 h , and then exceeded $58\text{S-}600^\circ\text{C}$ at 360 h . In addition, although the amount of silicon decreased with the increase of boron content in the bioglass materials, no great change was observed in the silicon concentration of solution. The above analysis illustrates that the doping of B facilitates the degradation of amorphous bioglasses and leads to a more stable degradation.

For the samples sintered at 800°C , the concentration of B in the SBF increased fast in the first 120 h , and then changed slowly during the simulated body fluid soaking experiment, as shown in Fig. 4(a). The boron content of the five samples heated at 800°C varied greatly, while the Si concentration did not change significantly with the different raw material ratio. And Si was released at a uniform rate. Although $58\text{S-}800^\circ\text{C}$ had no CaSiO_3 crystal, it had more Si in the glass grid structure and other four samples all contained CaSiO_3 crystal. Moreover, CaSiO_3 existed in B-doped bioglass powder and promoted the degradation of the bioglass-ceramic materials.

Fig. 3. Release of (a) B and (b) Si from samples sintered at 600°C for 3 h during immersion for 15 days in SBF.

Fig. 4. Release of (a) B and (b) Si from samples sintered at 800°C for 3 h during immersion for 15 days in SBF.

Fig. 5. Concentration comparison of B element in culture medium during the soaking in SBF of two groups of samples (a) 58S-B-1-600°C and 58S-B-1-800°C (b) 58S-B-2-600°C and 58S-B-2-800°C (c) 58S-B-3-600°C and 58S-B-3-800°C (d) 58S-B-4-600°C and 58S-B-4-800°C.

Figures 5 and 6 illustrate the concentration comparison of B and Si elements in the culture medium during the soaking in SBF of two series of samples, 58S-B-X-600°C and 58S-B-X-800°C. 58S-B-1-600°C released much more B than 58S-B-1-800°C, and with the increase of B in the material, the release rate of 800°C treated samples became

higher and the difference between two groups of samples became smaller. As for the silicon, the samples with same chemical constituents and different heat-treated temperature had similar Si release, while those heated at 800°C had a more stable release rate than the ones heat-treated at 600°C. The reason for the difference of B and Si release

Fig. 6. Concentration comparison of Si element in culture medium during the soaking in SBF of two series of samples (a) 58S-B-600°C and 58S-B-800°C (b) 58S-B-1-600°C and 58S-B-1-800°C (c) 58S-B-2-600°C and 58S-B-2-800°C (d) 58S-B-3-600°C and 58S-B-3-800°C (e) 58S-B-4-600°C and 58S-B-4-800°C.

Fig. 7. XRD patterns of the samples after immersion for 15 days in SBF (a) samples sintered at 600°C for 3 h, (b) samples sintered at 800°C for 3 h.

between two series samples is that Si entered in to the CaSiO_3 crystal structures with the 800°C heat-treatment, while B participated in the glass grid. Hence B was released to solution slowly. It is manifested that the sample with microcrystals has a lower degradation rate in the early stage, but the degradation amount in the subsequent stage is larger.

3.3 Characterization of samples after soaking in SBF

The bioglass and glass-ceramics shown in Figs. 7 and 8 were soaked in SBF for 15 days, then washed and dried, and then subjected to XRD and FTIR tests respectively. The XRD patterns illustrated in Fig. 7 show that only HA crystal orientation exists in the samples treated at 600 and

Fig. 8. FTIR of the samples after immersion for 15 days in SBF (a) samples sintered at 600°C for 3 h, (b) samples sintered at 800°C for 3 h.

800°C, and the characteristic peak intensity of HA is higher in Fig. 7(b), which indicates that the HA content is higher in samples treated at 800°C than the ones at 600°C. The sample heated at 800° contains calcium silicate crystals, and the calcium silicate crystal can release Si faster, which can promote the formation of HA. Comparing Fig. 1(b) with Fig. 7(b), it can be seen that the calcium silicate crystals in the samples before immersion in SBF disappeared when reacting with SBF during the soaking process and the characteristic peaks of HA are obvious.

Comparing the FTIR spectra of the samples before and after immersion, it can be seen that the structural changes of the 600°C sintered samples were relatively small. Since it had only one amorphous phase before soaking in SBF. Characteristic peaks of PO_4^{3-} in HA appeared in the XRD data after immersion, and two new broad peaks at 800 and 1100 cm^{-1} emerged in the picture, indicating a new Si-O bending. Data analysis states that the network structure of bioglass sintered at 600°C transformed, along with the production of HA.

As is shown that the doping of boron promotes the dissolution of silicon, which is an important step in the formation of HA. After 15 days of soaking, HA was produced in the bioglass powder. With the increase of B content, the HA formation decreased gradually and slightly. At the same time, the results of FTIR further explains the transformation of glass structure. The characteristic peak of Si-OH structure near 1000 cm^{-1} disappeared after soaking, and new peaks near 560, 600 and 1040 cm^{-1} appeared, which indicates the existence of PO_4^{3-} in HA. (in Fig. 8)

The $[\text{BO}_3]$ characteristic peak of the sample at 1400 cm^{-1} disappeared after immersion, and the peak at 1100 cm^{-1} became higher from sample 58S-600°C-3h-SBF to sample 58S-B-4-600°C-3h-SBF. While the peak of 1100 cm^{-1} includes P-O bond, Si-O bond and the B-O stretching in $[\text{BO}_4]$, which has been reported in literature as the characteristic peak of asymmetric stretching vibration of

B-O bonds from $[\text{BO}_4]$ units,³⁴⁾ so it can be presumed that the number of $[\text{BO}_4]$ structures increased at this point. Comparing with FTIR spectra of samples before soaking, a new band at 800 cm^{-1} appeared due to Si-O-Si stretching between tetrahedrals.³²⁾ The reason for the emergence of a new structure is that the unstable structures are more easily decomposed and dissolved in SBF during the soaking process, such as $[\text{BO}_3]$ and non-bridging oxygens (NBO) bond. At the same time, the glass structure was also changing constantly. More stable Si-O structure and B-O structure formed in this process, so the release rate of Si and B in the dissolution process was higher in the early stage, and then the concentration change became slower after a period of time.

For the sample treated at 800°C, a small amount of HA crystal was produced in the sample after heat treatment, and in addition to HA crystal, wollastonite crystal also appeared in the sample doped with B, as shown in Fig. 1(b). The FTIR results are consistent with the XRD result, and the characteristic peaks of PO_4^{3-} and calcium silicate appeared in the FTIR pattern [Fig. 2(b)] of the sample before immersion.⁴¹⁾ After immersion, there was only one crystal, HA, in the materials, while the characteristic peaks of CaSiO_3 disappeared. And all the peaks indicating the existence of HA became stronger in Figs. 7(b) and 8(b). Figure 7(b) shows the XRD pattern and Fig. 8(b) shows the FTIR data. The discussion above explains that samples containing B and microcrystals produced more HA, which declares that the material is more biologically active.⁴²⁾

3.4 Morphology analysis

SEM images of the 58S-B-1-600°C before and after immersion in SBF for 15 days and energy dispersive spectrometry (EDS) spectrum are shown in Fig. 9. Before soaking in SBF, bioglass existed in the form of irregular micro-nano particles, for the reason that the powder

Fig. 9. SEM images of the 58S-B-1-600°C before and after immersion for 15 days in SBF (a) before immersion, (b) after immersion, (c) EDS spectra of the sample called 58S-B-1-600°C after immersion in SBF for 15 days. Note the presence of Ca, P on the surface, $\text{Ca/P} \approx 1.67$.

material was made by grinding [Fig. 9(a)]. After soaking in SBF, the morphology of the surface changed, and some deposits appeared on the surface of the bioglass particles. The sediment was scaly, and it can be inferred that the sediment was HA based on the combined study of the XRD data, FTIR data and the literature report. EDS was used to further monitor the composite of formed HA on the surface of the bioglass materials. Figure 9(c) shows the EDS spectra of the sample called 58S-B-1-600°C after immersion in SBF for 15 days. The Ca and P peaks were detected and the atom ratio between Ca and P was 1.67, which was close to the ratio for the HA.

Figure 10 shows the SEM images of the 58S-B-2-800°C before and after immersion in SBF for 15 days and EDS spectra of the sample called 58S-B-2-600°C after immersion in SBF for 15 days. The bioglass powder before immersion in SBF was also irregular micro-nano particle, but the deposit after immersion in SBF was more compact than 58S-B-1-600°C. In addition, the Ca and P peaks in the EDS spectra were detected and the atom ratio between Ca and P was 1.62, which was also very close to the ratio for the HA.

The two sets of figures above illustrate the microscopic appearances of 58S-B-2-600°C and 58S-B-2-800°C before and after immersion in SBF for 15 days, and show the EDS of the samples after soaking. The two samples

described above are the representatives of the two series of samples with different heat-treatment temperature.

4. Conclusion

In this study, boron-doped bioactive glasses were prepared by the sol-gel method, and glass-ceramic materials containing calcium silicate microcrystals were obtained by heat treatment. The test results of the materials showed that doping of boron changed the glass net structure and promoted the formation of calcium silicate crystallites during heat treatment. Meanwhile, there was a small amount of HA in the material treated at higher temperature. The detection of boron and silicon content during the simulated body fluid immersion test result and performance testing results of materials after immersion showed that boron doping promoted the degradation of the glass material, although no crystallites were produced in the 600°C heat treated samples. Samples without B-doping contained only a small amount of HA crystal after heat treatment at 800°C. Nevertheless, the XRD patterns of boron-doped samples showed the characteristic peaks of CaSiO_3 , and the boron-doped samples produced far more HA than the samples without boron doping.

For silicate bioglass without boron, the bioactivity of the materials with no crystallites is higher than the glass ceramics. However, when treated by boron doping, lower

Fig. 10. SEM images of the 58S-B-2-800°C before and after immersion in SBF for 15 days (a) before immersion, (b) after immersion, (c) EDS spectra of the sample called 58S-B-2-600°C after immersion in SBF for 15 days. Note the presence of Ca, P on the surface, $\text{Ca/P} \approx 1.62$.

temperature heat-treated bioglass materials have higher degradation rate. When heat temperature becomes higher, boron can promote the production of CaSiO_3 crystals, thereby further improving degradation rate and the biological activity of the material.

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