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Effect of iron state on crystallization and dissolution in Fe_2O_3-CaO-SiO_2 glasses

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The possibility of iron-containing glasses as thermoseeds for hyperthermia of bone tumor was reported previously. There is, however, no report about the effect of iron state on the crystallization of magnetite and the resultant properties. The iron states were determined by Mössbauer spectroscopy in Fe_2O_3-CaO-SiO_2 system.

It was found that the higher CaO content interrupts the crystallization of magnetite crystallites as well as the oxidation of iron, that is, the transformation from Fe^{3+} to Fe^{2+}. A sample containing large amounts of Fe^{2+} showed the faster increment of temperature when the alternating magnetic field was applied. In order to use the thermoseed for a hyperthermia, we can say that the composition with low CaO content is most useful.

1. Introduction

It has been established that certain compositions of inorganic glasses form a mechanically strong bond with tissues [1, 2]. A common characteristic of these glasses is the formation of a hydroxyapatite layer at the interface between the implant and tissue. It is also known that bioactive glasses form a bond at a different rate depending upon their composition. A second common characteristic of the bioactive glasses is the formation *in vivo* of a silica-rich gel layer on the surface prior to or corresponding with the development of the interfacial apatite layer [3, 4].

It was reported [5], however, that P_2O_5-free CaO-SiO_2 glasses form an apatite layer on their surfaces in the body and bond to living bone through the apatite layer. On the basis of this result, it was previously shown [6] that a bioactive and ferrimagnetic glass-ceramic containing ferrimagnetic magnetite (Fe_3O_4) in a bioactive $CaO \cdot SiO_2$-based matrix is obtained by crystallization of $CaO \cdot SiO_2$-based glass containing appreciable amounts of Fe^{2+} and Fe^{3+} ions. Such bioactive and ferrimagnetic glass-ceramics might be used as thermoseeds for hyperthermia of cancer, especially such as a bone tumor. This possibility was first reported by Ebisawa *et al.* They studied the same molar ratio of SiO_2 and CaO in order to precipitate the β-wollastonite crystallites as an extention of A-W glass-ceramics.

In iron oxide containing glasses, the iron exists in primarily two oxidation states, namely, Fe^{2+} and Fe^{3+} states [7, 8]. These two states give rise to a characteristic magnetic effect. Therefore it is important to predict the possibility as thermoseed for hyperthermia of cancer. Little is known, however, about the effects of redox state of iron on the dissolution of iron containing glasses.

The purpose of this study was to investigate the role of the redox state of iron on the crystallization of magnetite and dissolution behavior of the glass compositions in Fe_2O_3-CaO-SiO_2 system.

2. Experimental method

2.1. Glass formation and heat-treatment

Powder mixtures of various compositions in Fe_2O_3-CaO-SiO_2 system were prepared from reagent grade chemicals, that is, SiO_2 (Junsei, Japan), $CaCO_3$ (Junsei, Japan) and Fe_2O_3 (Yakuri, Japan). They were put into a platinum-10% rhodium crucible, melted at 1550 °C for 2 h in a Kanthal Super furnace and poured onto a copper plate at 350 °C to be formed into a plate about 3 mm in thickness. After cutting into $10 \times 10 \times 2 mm^3$, polished surfaces with SiC papers and alumina powders to eliminate the contaminated surface layer by contact with the copper plate and washed with distilled water and alcohol.

Heat-treatment was carried out through controled nucleation and crystallization as previously reported [9, 10]. The nucleation and crystal growth conditions were 700 °C for 1 h and 1000 °C for 2 h, respectively.

2.2. Mössbauer spectroscopy

The redox state of iron was measured by Mössbauer spectroscopy (Austine Science, USA). γ-ray source was ^{57}Co of 10 m Ci diffused into the rhodium metal. γ-ray emitted from the source was absorbed by powder sample covered with aluminum foil and the intensity was detected by the proportional detector including cooling gases, i.e. CO_2 and CH_4.

2.3. Dissolution test

Dissolution test was carried out using powder glasses after grinding into $\sim 10\,\mu m$. 0.2 g of the glass samples were immersed into 90 ml of simulated body fluid (SBF) by Kokubo [6]. The fluid was buffered at pH 7.25 with 50 mM tris(hydroxymethyl)-aminomethane (NH2C[CH2OH]3) and 45 mM hydrochloric acid and the temperature was maintained at 37 °C. After soaking for a certain time, the concentrations of Si and Ca in the SBF solution were determined by ICP (Seiko, SPS 1200A, Japan).

2.4. MTT test

If the material is toxic to the cell, as are quartz crystal and asbestos fibers, the consequences are severe since the toxic material is repeatedly investigated by successive waves of macrophages and progressive fibrosis, known as silicosis or asbestosis [11]. MTT was carried out to detect the toxicity of the samples before and after heat-treatment after grinding into $\sim 10\,\mu m$. 1 g of powder samples were immersed into 10 ml of the Eagle's MEM nurture solution (Hazleton, Biologic Inc., USA). Then various concentrations of leaching solutions were extracted from the MEM nurture. After mixing with L929 cell, they were cultured at 37 °C for 48 h under 5% CO_2. The cultured solutions mixed up $50\,\mu m$ of MTT (-(4.5-dimethylthiazol-2-yl)-2.5-diphenyl-tetrazolium bromide). The concentrations of the L929 cells in the MEM nurture solution were measured with an ELISA reader (EL 308, Bio-Tek Instruments Inc., USA) with and without leaching solution. Relative growth rate (*RGR*) was calculated by the following equation.

$$RGR = (\text{Mean value in the experimental condition}/\text{Mean value in control}) \times 100 \quad (1)$$

3. Results and discussion

It was previously reported [9] that the hysteresis loss of the glass-ceramics is directly proportional to the magnetization saturation. Fig. 1 shows the change of magnetization saturation with the iron content. It can clearly be seen that the magnetization saturation is proportional to the iron content. Therefore it is important to glass formation with higher iron content. In the Fe_2O_3-CaO-SiO_2 system, glass can be formed up to 40 wt % of iron oxide. The glass transition and crystallization temperatures determined by dynamic thermal analysis (TG/DTA-92, Setaram, France) and density of the various compositions are listed in Table I.

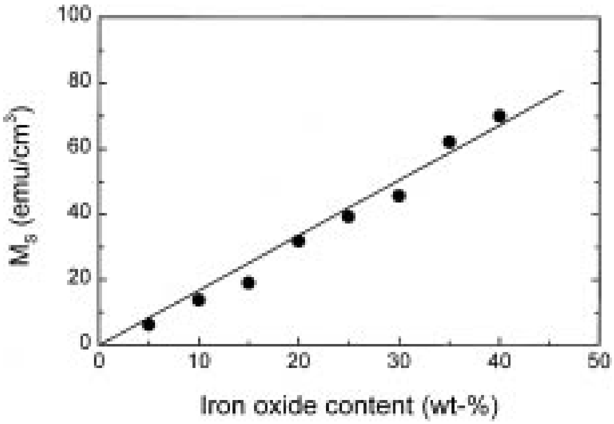

Figure 1 The change of magnetization saturation with Fe_2O_3 content.

In order to verify the effect of SiO_2/CaO ratio on the crystallization and dissolution behaviors, the ratios were varied between 0.5, 1 and 2. The oxidation states of the iron were determined by Mössbauer spectroscopy for samples A and B in Table I since the glass was devitrified during the quenching from melt when the ratio was 0.5.

The Mössbauer spectra of the as-prepared samples A and B are shown in Fig. 2a and B, respectively. These spectra do not exhibit the hyperfine splitting. This means the as-prepared samples are paramagnetic. Each ionic ratio of Fe^{2+} and Fe^{3+} states is presented in Table II. Sample A exhibited 2.7 times higher Fe^{2+} concentration than sample B. Fig. 3a and B show the Mössbauer spectra for samples A and B, respectively, heat-treated through controlled nucleation and crystallization at 700 °C for 1 h and at 1000 °C for 2 h. The hyperfine splitting appeared after heat-treatment because of the magnetite crystallites. The Mössbauer parameters, that is, isomer shifts, were 0.1343–0.5866, quadrapole splitting was 0.0010–0.1106 and hyperfine splitting was 457.17–518.24, showed reliable values compared with previously reported values [12–14]. Sample B exhibited two smaller peaks compared with sample A located in the center which represented paramagnetic. This means sample A has the smaller amount of precipitated magnetite than that of sample B. This could be due to β-wollastonite crystallites. Maybe the precipitation of β-wollastonite interrupts the precipitation of the magnetite crystallites. It was

TABLE I Chemical compositions and various properties of the samples

Sample code	Composition (wt %)	Temperatures (°C)			Density g/cm^3
		T_g	T_c	$T_c - T_g$	
A	40Fe_2O_3-20CaO-40SiO_2	612.0	858.5	246.5	3.38 ± 0.04
B	40Fe_2O_3-30CaO-30SiO_2	615.5	865.0	249.5	3.48 ± 0.04
C	30Fe_2O_3-25CaO-45SiO_2	655.0	873.5	218.5	3.12 ± 0.04
D	20Fe_2O_3-30CaO-50SiO_2	673.5	880.0	206.5	2.88 ± 0.03
E	10Fe_2O_3-35CaO-55SiO_2	710.0	905.0	195.0	2.63 ± 0.03

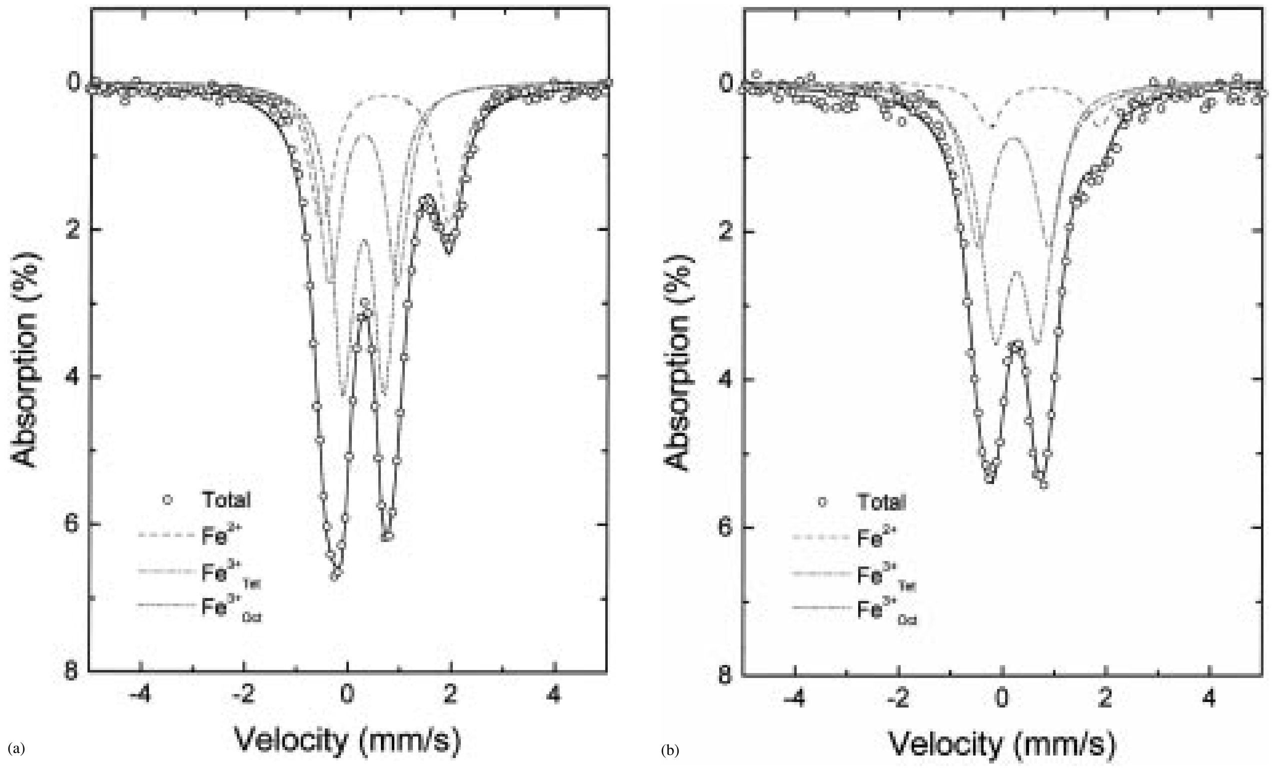

Figure 2 (a) Mossbauer spectrum of the as-prepared sample A and (b) sample B measured at room temperature.

TABLE II Ratio of iron states for the as-prepared glasses

Sample code	Fe^{2+}%	Fe^{3+}_{Tet}%	Fe^{3+}_{Oct}%
A	24.0	33.6	42.4
B	9.0	37.5	53.5

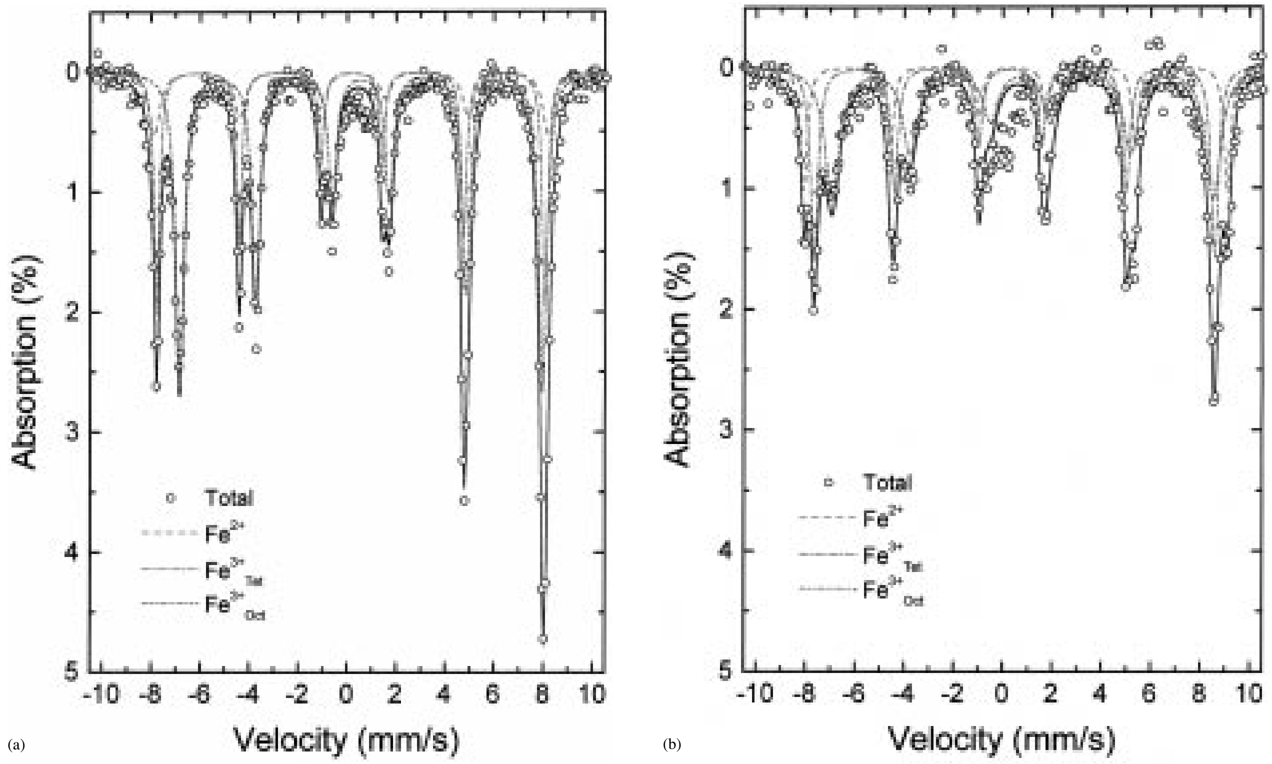

Figure 3 (a) The Mossbauer spectrum of the heat-treated sample A and (b) sample B measured at room temperature.

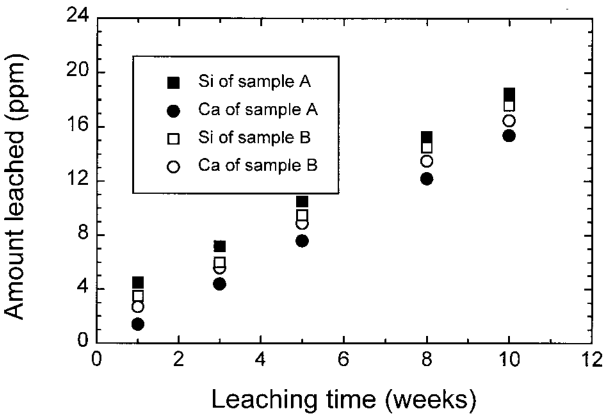

Figure 4 The amount of Si and Ca leached in SBF solution at 37 °C.

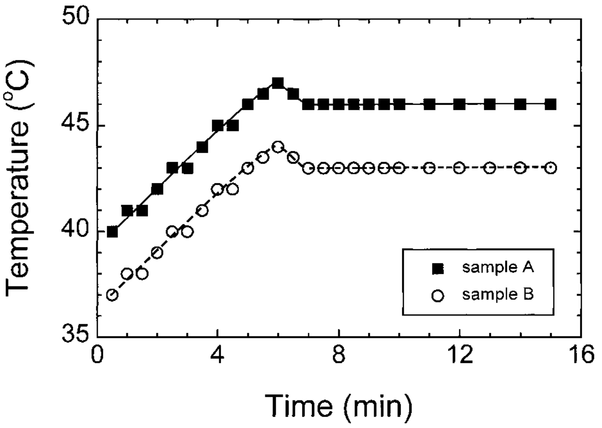

Figure 5 Change of temperature of sample A and B heat-treated at 700 °C for 1 h and at 1000 °C for 2 h under 10 kOe magnetic field and 10 kHz frequency.

TABLE III Relative growth rates by MTT test for as-prepared glasses and heat-treated samples

Sample	Time (d)	Concentrations of the leaching solutions			
		5%	10%	25%	50%
As-prepared Glass	2	90.5	87.8	67.9	69.4
	5	90.7	92.5	93.1	98.1
Heat-treated Sample	2	93.1	92.5	88.9	101.8
	5	88.6	71.9	74.9	85.8

found that smaller amounts of CaO are better for obtaining more magnetite crystallites.

The amounts of leached Si and Ca in SBF solution are shown in Fig. 4. Iron was not detected even after 10 weeks soaking in SBF in either sample A and B. The amounts of Si and Ca increased with leaching time and exhibited very low values. The maxima of Si and Ca were 18.5 and 16.5 ppm, respectively. It looks like iron oxide interrupts the dissolution of glass and glass-ceramics.

Table III shows the results of the MTT test. Relative growth ratio of the samples was above 80% in most cases. The samples could be biocompatible, however, long-term tests are necessary to apply clinical use.

Fig. 5 represents the rise in temperature of the heat-treated samples A and B at 700 °C for 1 h and at 1000 °C for 2 h under 10 kOe and 10 kHz of alternating magnetic field. It can be seen that both samples can be heated up to 43 °C, which is the effective hyperthermic temperature for cancer treatment, by 6 min after the magnetic field was applied, and this temperature was maintained as long as the magnetic field was applied. Sample A showed higher temperature than sample B. Maybe this is due to the large amount of magnetite crystallite as predicted by the Mössbauer spectra.

4. Conclusions

In order to observe the effect of SiO_2/CaO on the crystallization behavior and resultant properties, such as dissolution and biocompatibility, glasses were prepared with 40 wt % Fe_2O_3 and 1:2 SiO_2/CaO ratio.

It can be seen that the higher CaO content interrupts the crystallization of magnetite crystallites as well as the oxidation of iron, that is, the transformation from Fe^{3+} to Fe^{2+}. A sample containing large amounts of Fe^{2+} showed the faster increment of temperature when an alternating magnetic field was applied. In order to use the thermoseed for a hyperthermia, we can predict that the composition with low CaO content is more useful.

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