Studies on synthesis of calcium ferrite-based bio glass ceramics

B R JAGADISH, N PRABHU and D BAHADUR*

Department of Metallurgical Engineering and Materials Science, Indian Institute of Technology, Mumbai 400 076, India

MS received 9 January 1997

Abstract. The possibility of synthesizing a Ca-ferrite based biocompatible glass ceramic has been explored in the following two glass compositions: (i) $28\text{Na}_2\text{O}-8\text{CaO}-3\text{P}_2\text{O}_5-11\text{Fe}_2\text{O}_3-50\text{SiO}_2$, and (ii) $25\text{Na}_2\text{O}-8\text{CaO}-3\text{P}_2\text{O}_5-20\text{Fe}_2\text{O}_3-41\text{SiO}_2-3\text{B}_2\text{O}_3$ (in weight ratio). The effect of simulated body fluid on the different glasses and glass ceramics was also investigated. While there is no direct evidence for apatite formation, the weight losses recorded and formation of a Si-rich layer at the surface appears to be an indication of onset of apatite formation. The rate of apatite formation is presumably retarded due to the presence of Al^{3+} (picked up from Al_2O_3 crucible). Ferromagnetic resonance experiments at 9.03 GHz demonstrate that these glass ceramics can possibly be used for microwave hyperthermia.

Keywords. Bio glass ceramics; calcium ferrite; hyperthermia; apatite.

1. Introduction

It has been shown that bioactive glasses and glass ceramics bond to bone (tissue) by the formation of an apatite layer on the surface (Anderson *et al* 1990; Hench 1991; Ochura *et al* 1994). The apatite phase is equivalent chemically and structurally to the mineral phase of the bone and it is this equivalence which is thought to be responsible for the interfacial bonding (Hench 1991). The formation of surface apatite layer has been investigated by dipping the bioactive glasses and glass ceramics in a simulated body fluid (SBF) (with ion concentrations similar to those in human blood plasma) or in a Tris buffer solution (TBS) (Anderson *et al* 1990; Ebisawa *et al* 1990, 1992a; Kokubo *et al* 1992; Li *et al* 1992; Ohtsuki *et al* 1992).

A promising application of bioactive ferrite-based glass ceramics is in the hyperthermia treatment of cancer. On application of either an alternating magnetic field or microwaves, the bioactive magnetic glass ceramic acts as a localized heating target which leads to selective dissipation of heat to the cancerous tissues. Ebisawa *et al* (1992b) have successfully demonstrated the use of a bioactive ferrimagnetic glass ceramic (in $\text{Fe}_2\text{O}_3\text{-SiO}_2\text{-CaO-B}_2\text{O}_3\text{-P}_2\text{O}_5$ system) as a thermoseed for hyperthermia of cancer using an alternating magnetic field (the soft heating method). Ferromagnetic resonance (FMR) has been used by Nikawa and Okada (1987) for deep heating of the cancerous tissue for microwave hyperthermia. It was found that the energy dissipation rate at the target during FMR was 40% higher than that of nonresonance

microwave heating. Also, the depth of heating increased by nearly 50% at resonance.

In the present study our objective was to synthesize Ca-ferrite-based glass ceramics through nucleation and growth in $\text{CaO-Na}_2\text{O-P}_2\text{O}_5\text{-Fe}_2\text{O}_3\text{-SiO}_2$ -based glass. We have further evaluated the bioactivity of the different glass ceramics *in vitro* (using a TBS or a SBF solution). The different glass ceramics have been characterized in detail before and after treating them in SBF/TBS solution. The suitability for use as thermoseeds in microwave hyperthermia has been demonstrated by FMR studies.

2. Experimental

Two glasses G1 and G2 (compositions given in table 1), were prepared using reagent grade chemicals Na_2CO_3 , CaCO_3 , $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$, Fe_2O_3 , SiO_2 and H_3BO_3 . Melting was done in an alumina crucible and pouring of melts done at 1150°C and 1130°C respectively. The melt was splat quenched using two steel plates to obtain glass. XRD studies of powder samples were carried out on a Phillips PW480 diffractometer using CuK_α radiation in the scan range $20^\circ\text{--}100^\circ$.

Differential thermal analysis (DTA) was performed on the powder samples using a Dupont model 9900 system, with heating rate of 10°C/min in the temperature range

Table 1. Glass composite in weight percentage.

	Na_2O	CaO	P_2O_5	Fe_2O_3	SiO_2	B_2O_3
G1	28	8	3	11	50	—
G2	25	8	3	20	41	3

*Author for correspondence

20°C–1000°C. A typical DTA plot for glass (G1) is given in figure 1. The nucleation and growth temperatures were estimated from the DTA results and the glasses were accordingly subjected to different heat treatment schedules. The X-ray diffraction technique was used to determine the different phases that formed after heat treatment. Table 2 provides a list of various phases formed after different heat treatments.

TBS containing 50 mM Tris (hydroxymethyl) methylamine and 45 mM HCl was prepared as suggested by Anderson *et al* (1990) and Li *et al* (1992). Samples were dipped in 25 ml of TBS for a period of 30 days. SBF was prepared by dissolving reagent grade chemicals NaCl, NaHCO₃, KCl, MgCl₂ · 6H₂O, CaCl₂ · 2H₂O and CaHPO₄ · 2H₂O in distilled water. The solution was buffered by 50 mM Tris (hydroxymethyl) methylamine and 45 mM HCl (Ebisawa *et al* 1990, 1992a; Kokubo *et al* 1992; Ohtsuki *et al* 1992). Ion concentrations in SBF have been reported by Ohtsuki *et al* (1992). Samples were dipped in 50 ml of SBF each in stoppered standard flasks. In order to study modifications occurring at the surface, XRD studies were carried out on samples dipped in TBS and SBF. To study compositional changes occurring at the surface, energy dispersive X-ray (EDX) analysis was carried out on a few dipped and undipped

Figure 1. A typical DTA plot for glass G1.

samples. Cambridge Stereoscan 90B system was used for scanning electron microscopy (SEM). Ferromagnetic resonance studies of samples were done on a system using microwave frequency 9.07 GHz in scan range 0–4000 Oe magnetic field.

3. Results and discussion

The as-quenched glasses G1 and G2 are amorphous. Figure 2 gives the X-ray diffraction patterns of the glass G1 and the glass ceramics GC11 and GC14. While the

Figure 2. X-ray diffraction patterns of (a) glass G1, (b) GC11 and (c) GC14.

Table 2. Heat treatment, label and crystalline phases observed.

Glass ceramic	Starting glass	Heat treatment		Crystalline phases present
		Nucleation	Growth	
GC11	G1	430°C/1 h	780°C/24 h	CaFe ₄ O ₇ , α-Fe ₂ O ₃ (MR)
GC12	G1	730°C/1 h	780°C/24 h	CaFe ₄ O ₇ , α-Fe ₂ O ₃ (MJ)
GC13	G1	430°C/1 h	740°C/24 h	CaFe ₄ O ₇
GC14	G1	430°C/1 h	780°C/48 h	CaFe ₄ O ₇
GC21	G2	475°C/1 h	690°C/24 h	CaFe ₄ O ₇ , α-Fe ₂ O ₃ (MJ)
GC22	G2	570°C/1 h	883°C/24 h	CaFe ₄ O ₇ , α-Fe ₂ O ₃ (MR)

MJ = major, MR = minor.

sample G1 is completely glassy in nature, the sample GC11 exhibits XRD lines of both CaFe_4O_7 and $\alpha\text{-Fe}_2\text{O}_3$ phase. But, when the growth time is increased from 24 h to 48 h, as in the sample GC 14, a single CaFe_4O_7 ferrite phase is obtained. It is possible that with increase in growth time $\alpha\text{-Fe}_2\text{O}_3$ reacts with CaO in matrix phase by the following reaction:

Based on the results shown in table 2 we have observed that when the nucleation temperature is increased from 430°C to 730°C as in GC12 sample, a higher relative amount of $\alpha\text{-Fe}_2\text{O}_3$ is obtained. This suggests that 430°C is the right nucleation temperature for Ca-ferrite phase.

Figure 3. Scanning electron micrographs of glass ceramic samples a. GC12 and b. GC21.

while 730°C represents the nucleation temperature for $\alpha\text{-Fe}_2\text{O}_3$ phase. Further, when the growth temperature was decreased to 740°C from 780°C as in GC13 sample, a single CaFe_4O_7 phase was obtained with low glassy background. This indicates that 740°C is an optimum growth temperature for CaFe_4O_7 phase. The GC21 and GC22 samples show both the crystalline phases i.e. CaFe_4O_7 and $\alpha\text{-Fe}_2\text{O}_3$. The relative amount of $\alpha\text{-Fe}_2\text{O}_3$ phase is greater in GC21 than in GC22 sample.

These results from X-ray diffraction studies are supported by scanning electron micrographs. It can be seen for sample GC12 in figure 3a, that there is a distinct tendency for the second phase to separate as non spherical structure with high connectivity and dendritic growth. There is also a clear evidence for the existence of two phases in the sample GC21 as seen from figure 3b. The heat treatment process presumably allows enough time for glass in glass phase separation followed by crystallization of CaFe_4O_7 and $\alpha\text{-Fe}_2\text{O}_3$.

Weight losses were recorded after dipping the glass and glass ceramic samples either in TBS or SBF solution for varying duration. Table 3 gives the weight losses in mg/g for the different samples. From this table it can be seen that glass suffers a weight loss of 1–2 orders of magnitude less than that suffered by the glass ceramics. This is in accordance with the results published in literature which suggest that presence of Fe_2O_3 in a glass improves its stability (Ochura *et al* 1994). On heat treatment, Fe_2O_3 presumably enters the crystalline phase, and the residual glassy phase becomes less stable.

For GC11, GC12 and GC13, the weight loss increases with increasing degree of crystallinity (weight loss by $\text{GC13} > \text{GC11} > \text{GC12}$). This indicates that greater the extent to which crystallization occurs, the better is the removal of Fe_2O_3 from glassy phase and hence more unstable is the glassy phase.

Figure 4 gives the X-ray diffraction patterns of some typical samples GC21, GC21D, GC11D and GC13D. The dipped samples are represented by adding letter D in their label. XRD patterns of samples dipped in TBS/SBF reveal formation of an amorphous surface layer

Table 3. The weight losses for different samples.

Sample	Weight loss (mg/g)	
	In TBS after 30 days	In SBF after 8 days
G1	0.344	—
G2	—	1.04
GC11	26.42	—
GC12	19.84	24.86
GC13	30.19	12.92
GC14	16.19	—
GC21	—	15.49
GC22	—	25.97

Figure 4. Typical X-ray diffraction patterns of samples (a) GC21, (b) GC21D, (c) GC11D and (d) GC13D. D refers to samples dipped in TBS/SBF.

in some cases (i.e. GC12D, GC14D, GC21D, GC22D). On the other hand, there is formation of a crystalline surface layer as in the sample GC11D. The sample GC13D, however remains essentially unmodified except small shift in d values. The crystalline surface layer on GC11D could not be identified.

Modification of the surface is observed only in cases where an appreciable amount of glassy phase is present (as in GC11, GC12 and GC14). When crystallization has proceeded to a large extent as in GC13, we see no surface modification. This seems to be in agreement with Li *et al* (1992), who showed that residual glassy phase in a glass ceramic is responsible for the surface

Figure 5. Scanning electron micrograph of sample GC11D.

Figure 6. Ferromagnetic resonance spectra for samples GC13 and GC11.

modification and an apatite layer formation. Their results show that bioactivity is lost when residual glassy phase is less than 5 wt%. Glass G1 which showed negligible weight loss, shows no surface modification.

Since we could not identify the crystalline phase developed at the surface of GC11D, we attempted to probe the composition of the surface of dipped and undipped samples of GC11 by EDX. These results indicated that the concentration of sodium on the surface decreases from 22.3% to 1.43% on dipping, while the concentration of Si in the surface increases from 48.5% to 66.3% on dipping. According to Hench (1991), Na depletion at the surface along with the formation of a Si-rich layer, is the first step in the formation of an apatite layer on the surface of bioactive glasses and glass ceramics. EDX analysis shows the presence of aluminium picked up from the alumina crucible. It seems to have occurred during preparation of the glass. Earlier work (Anderson *et al* 1990; Kokubo *et al* 1992; Ohtsuki *et al* 1992; Ochura *et al* 1994), have shown that presence of Al retards bioactivity. Anderson *et al* (1990) suggest that presence of Al in the silica-rich layer retards the formation rate of apatite layer and also stabilizes the glass, thus preventing formation of a CaO-P₂O₅-rich film on top of the Si-rich layer. This could be the reason why only a Si-rich or an amorphous layer is observed in our case without formation of an apatite layer. SEM micrographs of the sample GC11D shown in figure 5, exhibits fibrous crystals which appear oriented perpendicular to outer surface. Presumably, the apatite starts nucleating and growing from these silica-rich fibrous grains (Ebisawa *et al* 1992b).

A ferromagnetic resonance experiment at 9.07 GHz and magnetic field up to 4000 Oe was done on a few samples just to demonstrate absorption of microwave power by the sample. We get broad resonance for GC13 as shown in figure 6. GC11 shows much broader and two resonances at fields of 1540 and 3100 Oe. The

evidence of absorption of microwave power and the resonance indicates that these glass ceramics can possibly be exploited for microwave hyperthermia using ferromagnetic resonance.

We have explored the formation of bioactive ferrite-based glass ceramics in Na₂O-CaO-P₂O₅-SiO₂-Fe₂O₃-based system and examined the possibility of apatite formation on the surfaces of glass ceramics in SBF/TBS solution. Further, absorption of microwave power has been demonstrated through ferromagnetic resonance.

Acknowledgement

Financial support from CSIR, New Delhi is gratefully acknowledged.

References

- Anderson O H, Liu G, Karlsson K H, Niemi L N, Miettinen J and Juhanaja J 1990 *J. Mater. Sci.: Mater. Med.* **1** 219
- Ebisawa Y, Kokubo T, Ohura K and Yamamuro T 1990 *J. Mater. Sci.: Mater. Med.* **1** 239
- Ebisawa Y, Kokubo T, Ohura K and Yamamuro T 1992a *J. Mater. Sci.: Mater. Med.* **4** 225
- Ebisawa Y, Murashita T, Kokubo T, Ohura K, Ikenaga M, Yamamuro T, Hiraoka M and Abe M 1992b *Proc. of the sixth int. conf. on ferrites (ICF6)*, Japan (Japan: Society for Powder and Powder Metallurgy) p. 287
- Hench L L 1991 *J. Am. Ceram. Soc.* **74** 1487
- Kokubo T, Kishitani H, Ohtsuki C, Sakka S and Yamamuro T 1992 *J. Mater. Sci.: Mater. Med.* **3** 79
- Li P, Yang Q, Zhang F and Kokubo T 1992 *J. Mater. Sci.: Mater. Med.* **3** 452
- Nikawa Y N and Okada F 1987 *IEEE Trans. Magn.* **23** 2431
- Ochura K, Nakamura T, Yamamuro T, Ebisawa Y, Kokubo T and Oka M 1994 *J. Mater. Sci. Mater. Med.* **3** 95
- Ohtsuki C, Kokubo T and Yamamuro T 1992 *J. Mater. Sci.: Mater. Med.* **3** 119