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The stability of hydroxyapatite in an optimized bioactive glass matrix at sintering temperatures

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The stability of sintered hydroxylapatite particles was studied in glass matrices of the system SiO_2–CaO–P_2O_5–Na_2O–Al_2O_3–B_2O_3 at sintering temperatures between 700 and 1000 °C. The results from X-ray diffraction (XRD), scanning electron microscope (SEM), energy dispersive spectroscopy (EDX) analysis, transmission electron microscopy (TEM) and electron diffraction showed that above 700 °C the Na^+ ions diffuse into the hydroxylapatite particles which then transform into rhenanite. The glass matrix undergoes crystallization yielding wollastonite crystals and a silica rich matrix.

1. Introduction

During the last few decades a class of new materials has evolved in the glass and ceramic field with exciting biological properties. These materials have been called bioactive or surface reactive on account of their ability to allow bone to grow and attach onto their surfaces. Perhaps the best way to divide these materials is by their structural and compositional differences: Ca–P ceramics (ceramics consisting of oxides of Ca and P, e.g., hydroxylapatite, α and β-tricalciumphosphate), bioactive glasses (surface active glasses that form protective silica and calciumphosphate surface layers) and bioactive glass-ceramics (crystallized glasses that have a similar surface active property as glasses). These groups of materials have both mechanically and biologically widely varying properties, that will not be fully accounted for in this paper.

Our attention will be focused to certain relevant characteristics of hydroxylapatite (HA), bioactive glass and the apatite–wollastonite (A–W) containing glass-ceramics.

The reaction of HA in the body differs from the rest of the bioactive materials, in that, it is a fairly inert material in aqueous solution whereas the others exhibit a strong yet controlled ion release in solution.

After a period of time *in vivo*, HA may have degraded from its surface up to some tens of micrometres. When applied as a thin coating such degradation may lead to an eventual loss of the complete layer. Glasses, instead of losing volume, create a weak Si-rich layer which for an unknown reason is able to act as a substrate for the calciumphosphate precipitation. In push out tests the failure has often occurred along the Si-rich layer [1].

The apatite–wollastonite glass-ceramics have been reported to obtain the highest bone bonding strengths [2]. It may be assumed that this is due to the strengthening factor of the crystals in the reaction layer at the surface. However it has not yet been attempted to optimize the bioactive properties of this kind of glass-ceramics.

It is hoped that by obtaining a material composed of an optimized bioactive glass phase and of sintered HA, the following questions could be answered in future research:

1. What effect would HA particles have on the formation and functioning of the Si-rich layer?
2. How would HA particles effect the formation of the Ca–P layer in solution at the surface of the material?

The primary aim of this study was to produce a composite material out of HA + bioactive glass, *via* a simple sintering process in a dense form. In this article the results of the study of the reactions of the hydroxylapatite particles with the glass matrix at elevated temperatures are presented.

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TABLE I Compositions of glasses used (wt %)

Glass	SiO_2	Na_2O	CaO	P_2O_5	Al_2O_3	B_2O_3
54S2.5	53.9	27.49	12.41	6.2	–	–
53S5	52.57	25.8	13.13	3.23	2.00	3.28
55S3.7	55.45	23.7	13.09	4.5	0.52	0.052
55S7.4	55.0	21.0	17.5	3.0	0.5	3.0
49S14.3	48.5	27.0	22.5	2.0	–	–

2. Materials and methods

2.1. Material design

Three glasses (54S2.5, 53S5 and 55S3.7) used for the preparation of the composite materials were designed using a computer based optimization program [3] that utilized a set of phenomenological equations (developed by Ö. Andersson) describing the influence of the glass composition on the following properties of the SiO_2–Na_2O–CaO–P_2O_5–B_2O_3–Al_2O_3 glass system [4]: The glass transition temperature (T_g), the thermal expansion coefficient (α), durability in solution (P_{98}) and bone bonding properties (MB). The glass compositions were optimized with respect to three of these properties, i.e., T_g, α and MB.

The glass compositions used in this study are listed in Table I. The properties of the glasses are shown in Table AI in the Appendix. Glasses 49S14.3 and 55S7.4 were used initially for the development of the above mentioned equations and were used in this study in the preliminary stages.

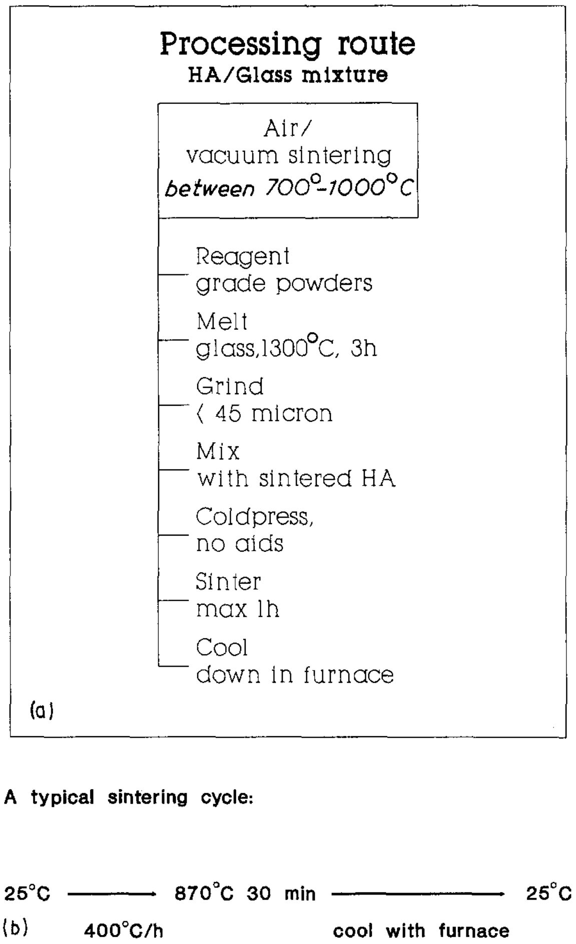

Figure 1 Schematic production route of the composite materials.

2.2. Material preparation

The glasses were prepared from analytic grade chemicals (SiO_2–Na_2CO_3–$CaCO_3$–P_2O_5–B_2O_3–Al_2O_3) by melting at 1300 °C for 3 h in a platinum crucible and quenching in deionized water. Resulting glasses were ball-milled with absolute ethanol for at least 3 h and then sieved with a stainless steel sieve to below 45 μm size. This powder was then mixed with ground hydroxylapatite powder (sintered at 1250 °C, dense) of two different particle sizes, i.e., those of $x < 45$ μm and $125 < x < 150$ μm. Mixing was done in a dry mill for at least 1 h. The mixed powders were cold dry-pressed into pellets 1.3 cm in diameter and 1.5 mm thick under about 100 MPa and then sintered in air or vacuum between temperatures of 850°–1000 °C for between 15 min and 1 h. The production route is shown schematically in Fig. 1a and b.

2.3. The evaluation of the materials

The effect of sintering time and temperature were studied on the crystal and micro structure of the material by SEM, TEM and XRD (also using a hot camera).

Two glass (49S14.3 & 55S7.4)/HA mixtures were examined using an XRD (Philips) system equipped with a hot camera. The temperature was increased at approximately 300 °C h^{-1} up to 1000 °C. The relative intensity of the peak from the (2 1 1) plane of HA was measured and plotted against the temperature.

The crystal structure of the other glass/HA mixtures were measured at room temperature.

Samples for the scanning electron microscopy were ground from the surface in an angle of approximately 30° or 90° by hand, polished (3 μm) and coated with carbon or gold. Backscattered and secondary electron imaging were used and some samples were analysed with EDX installed in the Cambridge 200 SEM.

One sample of glass 55S7.4/HA (870 °C, 15 min) was ion-mill thinned and studied using TEM and selected area electron diffraction.

3. Results

3.1. High temperature X-ray diffraction

The hot camera XRD experiment with glass 49S14.3 and 55S7.4 mixed with HA powder (calcined at 800 °C) showed that HA is relatively stable up to a temperature of around 850 °C, above which the HA peaks vanish fast (in less than an hour). Fig. 2 shows the plot of HA (2 1 1) plane diffraction peak intensity against the time/temperature of glass 49S14.3/HA and glass 55S7.4/HA mixtures. These figures are not necessarily representing equilibrium states since the heating rate was fixed and thus the reaction time remained short at each temperature.

On the basis of these measurements it was decided to attempt sintering between 700–1000 °C for various times with different mixtures.

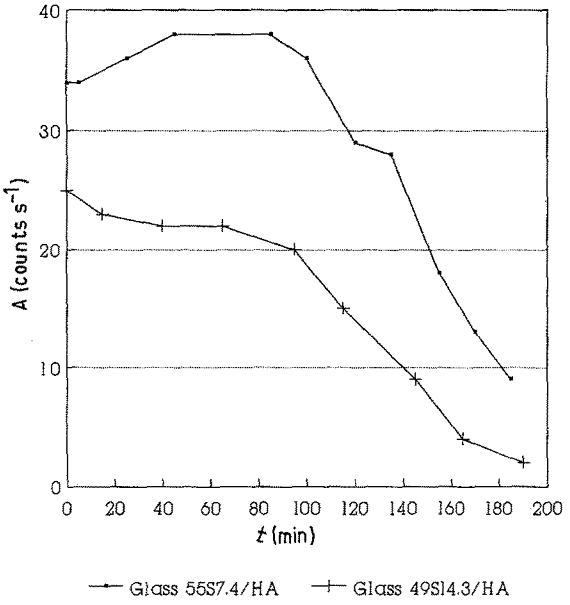

Figure 2 Hot camera X-ray diffraction of mixtures of HA with glass 55S7.4 and glass 49S14.3. The intensity of the HA 2 1 1 plane diffraction peak was measured as a function of time/temperature. The temperature was increased at a rate of approximately 5 °C min^{-1} up to 1000 °C.

3.2. Room temperature X-ray diffraction

Generally, the following reaction was observed during sintering independent of the glass composition or of the size ($x < 45$ µm or $125 < x < 150$ µm) and content (1:1 or 7:3 glass to HA weight ratio) of the hydroxylapatite particles in the composite:

$$\text{HA} + \text{glass} \rightarrow \text{Rh} + \text{Wo} + \text{glass (Si–rich)}$$

where HA = $Ca_{10}(PO_4)_6(OH)_2$ (hydroxylapatite); Rh = $CaNaPO_4$ (β–rhenanite); Wo = $CaSiO_2$ (wollastonite); Glass = SiO_2–CaO–P_2O_5–Na_2O–(B_2O_3)–(Al_2O_3).

After a sintering time of 1 h at 1000 °C this reaction was still incomplete and three crystalline phases were observed. This reaction was observed also at the lowest sintering temperature of 700 °C.

From the relative diffraction peak intensities it was found that the growth of rhenanite peaks were complimentary to the reduction of the HA phase. The rhenanite was identified as the low temperature β–rhenanite form which is stable below 650 °C in a pure form. Wollastonite peaks seemed to develop slightly slower.

3.3. SEM and TEM

With backscattered electrons imaging four different phases were detected in the microstructure of the specimens listed in Table II. These phases could be seen with the backscattered electrons imaging shown in Figs 3 and 4. EDX analysis showed the phases to be close in composition to HA, Wo and Rh irrespective of the sintering conditions (Table II). The glass phase composition greatly increased in SiO_2 content as sodium was drawn out by the hydroxylapatite particles. The volume next to the surface inside the HA

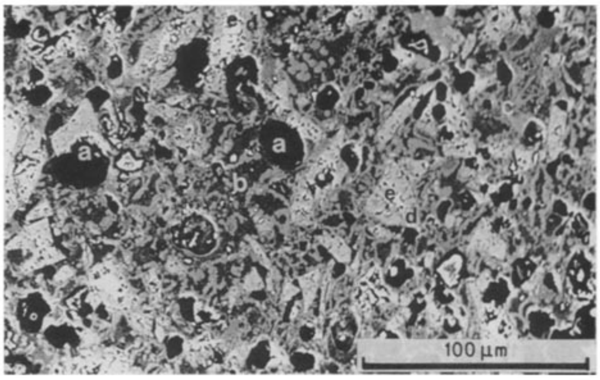

Figure 3 A backscattered electron image of the bulk cross-section of a sample with glass 54S2.5 + HA particles of 125–150 µm size in 7:3 weight ratio. Sintered at 850 °C for 1 h. Four different phases are visible: A: Pores (black), B: Glass phase (dark), C: Wollastonite crystals (medium darkness), D: Rhenanite (light), E: Hydroxylapatite particle centre (white). At 850 °C after 1 h the distance of sodium diffusion in HA is about 10–15 µm.

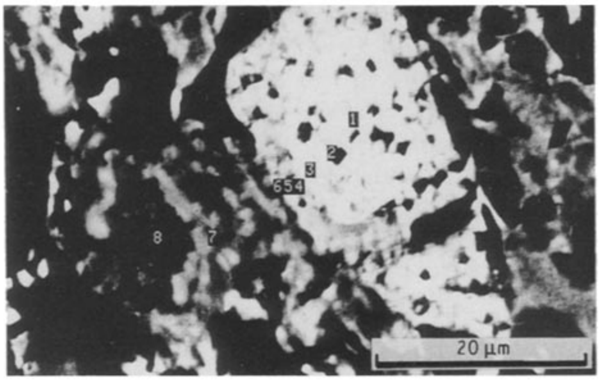

Figure 4 A backscattered electron image of the bulk cross-section of a sample with glass 54S2.5 + HA 125–150 µm after 1 h at 850 °C in vacuum. The numbers indicate the locations where the EDX point analyses were performed. Code: 1–3: Hydroxylapatite, 4–6: Rhenanite, 7: Wollastonite, 8: glass.

TABLE II Phases that were observed with XRD and their approximate compositions (wt %) as measured with EDX analysis. Material column shows: Glass type, HA particle size, glass/HA ratio (wt %), sintering temperature and time

Material	Phases	SiO_2	CaO	P_2O_5	Na_2O
54S2.5/125	HA[a]	–	–	–	–
7:3	Glass	75	10	1	9
850 °C	Wo	45	30	10	13
1 h	Rh	1–4	39	40–50	14
54S2.5/125	HA	0	54	44	0
7:3	Glass	72	13	5	9
850 °C	Wo	50	29	9	12
vacuum	Rh	2	38	44	15
1 h					
55S7.4/45	HA[a]	–	–	–	–
1:1	Glass	80–85	8	2	6
1000 °C	Wo	47	42	6	2
1 h	Rh	1	32	46	19
55S3.7/125	HA	0	48	50	1
2:1	Glass	72	10	5	11
850 °C	Wo	50	23	5	20
vacuum	Rh	0–7	30–40	40–50	7–20
0.5 h					

[a] detected with X-ray diffraction but not with SEM.

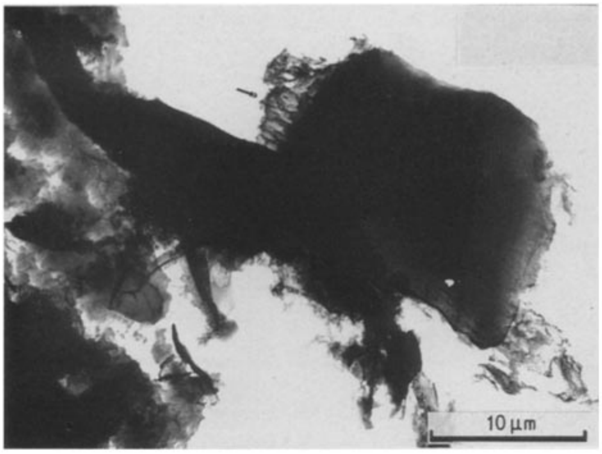

Figure 5 A TEM image of a HA particle and wollastonite crystals growing from its surface (arrow). Original magnification 4000 × . Sample: Glass 55S7.4 + HA 125–150 µm, 1:1 Wt ratio, 870 °C, 15 min.

particles had become rich in Na_2O and was close in composition to Rh. Crystals in the glass phase were shown to resemble the composition of Wo.

A similar structure was observed with TEM. The *d*-spacings of the crystal structures observed in the glass matrix of a sample sintered at 850 °C for 15 min (55S7.4/HA, 1:1, 125–150 µm) were calculated from the selected area electron diffraction images and were found to be close to those of wollastonite (Fig. 5).

4. Discussion

The following model is proposed for the reactions between HA and glass (Fig. 6): The sodium ions diffuse from the glass phase into the hydroxylapatite structure which then transforms into rhenanite. The diffusion process is not extremely fast and with sufficiently short reaction times the sodium ions had not reached the centres of the HA particles. The observed compositions of the HA particles give a Ca/P ratio lower than 1.67 indicating that some reaction has already taken place leading to a Ca deficient apatite structure even before the Na^+ ions have penetrated the material.

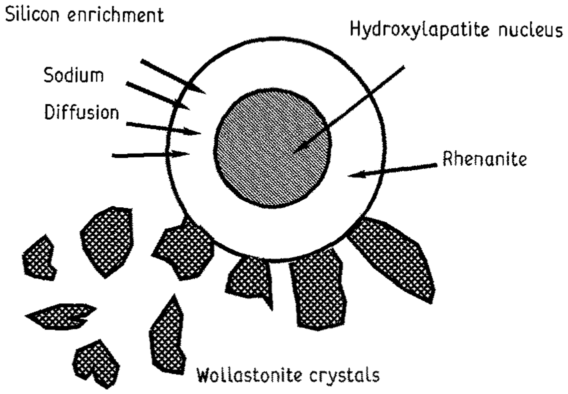

Figure 6 Schematic representation of the reactions occurring between the glass matrix and the hydroxylapatite particles. Na^+ ions diffuse into the HA particles which subsequently transform into the rhenanite. Hydroxylapatite ceases to exist as the Na ions completely penetrate the particles. Simultaneously wollastonite crystals nucleate and grow in the glass matrix and on the surfaces of the HA particles.

Wollastonite crystals nucleate and grow in the glass phase and onto the surfaces of the HA particles. Phosphour atoms seem to be incorporated in the wollastonite lattice. In the early stages of crystal growth Na ions are also incorporated in the Wo crystals. The remaining glass phase was sodium depleted and had an increased silica content up to about 80% (in 1 h at 1000 °C).

Rhenanite is a compound that has been used as a fertilizer due to its high solubility and, recently, Ramselaar *et al.* have published data [5] describing its behaviour *in vivo*. They found rhenanite to be bioactive in the same way as hydroxylapatite or tricalciumphosphates, but also exhibiting a high solubility in body environment, the rate depending on location and cell activity.

Thus from the biological point of view it would not matter whether the calciumphosphate-ceramic particles in the glass matrix were hydroxylapatite or rhenanite. On the contrary it would probably be beneficial to have a higher initial Ca and P ion release from the material preceeding the recrystallization of hydroxylapatite onto the surface of the material. If one would take rhenanite particles as a starting material then the remaining problem would be the changes in the glass composition during sintering. Currently, we are studying the reactions between rhenanite and the optimized glasses during sintering. Clearly the controlling factor for the successful production of this kind of material is the succesful prevention of the sodium diffusion into the HA particles, as, for instance by the incorporation of fluorine [6]. In that case the hydroxylapatite transforms into fluorapatite. Thus it seems that it is not possible to produce hydroxylapatite containing glass composites in this temperature regime. Also other calcium phosphate ceramics have been shown to be vulnerable to the presence of sodium. In various phase diagram studies, which involved some Ca–P ceramic together with Na_2O, rhenanite, was always found to exist in equilibrium with some other Ca–P ceramic phase [7–9].

However from the hot camera XRD curves we concluded that below a certain temperature the diffusion of sodium ions is insignificant and we already confirmed this by a simple sintering experiment at 600 °C for 480 min of the 54S2.5/HA < 45 µm material. The room temperature X-ray revealed no changes in the crystal structure of the resulting material. Our current efforts are directed to the production of dense composite materials in this low temperature regime.

5. Conclusions

It has been shown that, in the SiO_2–CaO–P_2O_5–Na_2O glass system hydroxylapatite is not stable above 700 °C. Sodium diffuses from the glass matrix into the hydroxylapatite particles and a phase transformation occurs yielding a hexagonal β-rhenanite structure. The glass phase partially crystallizes into wollastonite, which also incorporates phosphour and sodium atoms, leaving the glass matrix high in silica content.

A normal sintering process (above 700 °C) does not lead to a composite containing hydroxylapatite in the

SiO_2–CaO–P_2O_5–Na_2O glass system but to a composite containing rhenanite particles in a glass matrix of uncontrolled composition that has partially crystallized into wollastonite. From the materials science point of view the essence of these conclusions is two-fold:

1. The hydroxylapatite particles do not remain hydroxylapatite.
2. The properties of the glass matrix change from the optimized values to unknown values due to the changes in composition.

In other words the sintering procedure above700 °C is useless because of the reaction occurring between HA and the glass matrix. On the other hand at 600 °C no reactions were observed which allows for the possibility of successful production of a composite material composed of HA and optimized glass.

From the point of view of making a composite coating onto a metal substrate by means of plasma spraying, we do not expect the phase transition to occur due to the very short times that the particles are exposed to high temperatures. It may be assumed that the reaction time remains so short that the sodium ions do not have enough time to diffuse excessively into the HA particles.

Appendix

In Table AI glass 54S2.5, 53S5 and 55S3.7 based on the optimization programme 49S14.3 and 55S7.4 were used to develop the equations for the optimization programme. The bone bonding is defined as the percentage of matured bone developed in contact with the implant of the projected area of the cortex onto the surface of the implant. The corrosion is defined as the volume of 0.01 HCl (ml) needed to neutralize the leaching solution used per gram glass after 1 h in demineralized water at 98 °C.

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TABLE AI Properties of the glass compositions used

Glass	Bone bonding		T_g(°C)		$\alpha T[10^{-9}]$	Corrosion	Viscosity		Log dPas	@ 800 °C
	X	*Y*	*X*	*Y*	*X*	*Y*	*X*	*Y*	@ 600 °C	
54S2.5	100	–	399	490	1.352	–	2.942	–	4.518	1.98
53S5	100	–	389	–	1.319	–	7.746	–	2.768	0.748
55S3.7	–	–	420	–	1.215	–	2.020	–	–	–
55S7.4	98	–	–	525	–	1.18	–	0.56	–	–
49S14.3	82	–	–	–	–	1.30	–	1.93	–	–

where *X*: Calculated result and *Y*: Measured result.