JOURNAL OF MATERIALS SCIENCE: MATERIALS IN MEDICINE 1 (1990) 219–227

In vivo behaviour of glasses in the SiO_2–Na_2O–CaO–P_2O_5–Al_2O_3–B_2O_3 system

Ö. H. ANDERSSON, GUIZHI LIU*, K. H. KARLSSON
Department of Chemical Engineering, Åbo Akademi, SF-20500 Åbo/Turku, Finland

L. NIEMI, J. MIETTINEN
Institute of Dentistry, University of Turku, SF-20520 Åbo/Turku, Finland

J. JUHANOJA
Laboratory of Materials Science, University of Turku, SF-20520 Åbo/Turku, Finland

Sixteen glasses in the SiO_2–Na_2O–CaO–P_2O_5–Al_2O_3–B_2O_3 system were studied. The glasses were implanted in rabbit tibia. According to their *in vivo* behaviour, they were divided into five groups. A phenomenological equation for the *in vivo* behaviour was developed. The solubility of the glasses was determined *in vitro* as weight loss in Tris buffer solution. The tissue response is discussed in relation to the glass composition and the solubility. For bone-bonding glasses calcium phosphate formation takes place within a silica-gel at the glass surface. The gel must be sufficiently hydrated and flexible to allow calcium phosphate to build up. The results suggest that alumina can inhibit bone bonding by retarding the formation rate of a silica-rich layer, by stabilizing the silica structure enough to prevent calcium phosphate build-up within the layer, or by either disturbance of the bone mineralization or bone incompatibility of an alumina-containing calcium- and phosphorus-rich surface layer. The mechanism responsible for the lack of bone adherence is determined by the glass composition. Up to about 1.5 wt% Al_2O_3 can be included in the glass without destroying the bioactivity.

1. Introduction

Bioactive glasses adhere to bone through a chemical bond [1]. This property makes them interesting in bond replacement. Hench [2] has described the bonding mechanism as a sequence of reactions between the glass and the surrounding fluid. Gross and Strunz [3] described the bonding from a biological point of view. The net result of the bonding reactions is the formation of a silica-rich layer and on top of this, a calcium- and phosphorus-rich layer which is firmly attached to the bone. One of the problems associated with the use of these glasses is their high solubility, which may reduce their long-term reliability. To a certain limit a higher solubility results in a higher bioactivity. The traditional way to control the solubility of glass is by Al_2O_3 additions. It is, however, well known that alumina addition may inhibit the bone bonding [3–5]. Gross and Strunz [3] showed that the bone mineralization was disturbed in the presence of glasses containing a combination of Al_2O_3 and Ta_2O_5. The Al_2O_3 content was 7.5 to 15 wt %. In previous study it was found that about 1.5 wt % Al_2O_3 could be used without interfering with the mineralization of osteoid [5].

In designing glass compositions certain requirements must be considered. Often the development of glasses possessing specified properties is based on experience and trial-and-error. However, several physical properties of glass may be described as a function of their composition. The description may be based, at least to some extent, on structural considerations, e.g. Appen's method [6] for estimating the thermal expansion. From a practical point of view, however, a phenomenological model is equally useful. In a previous work phenomenological models for the bone contact as well as for some physical properties were presented [5]. The use of an optimization program makes it possible to design glasses possessing certain specified properties. In the model for the tissue response, the bone contact was expressed as the glass surface covered by bone after 8 weeks in rabbit tibia. For the physical properties, models with regression coefficients of about 99.9% were obtained. Due to the large scatter in the results, the model for the bone contact had a regression coefficient of only 89.0%. The standard deviation for the percentage mature bone was as high as $\pm$ 15.6%. The model may be used in optimizing bioactive glasses, although it is quite approximate and expresses only the bone contact, not the bonding. In the present work the compositional limits were extended and the purpose was to develop a better model for the *in vivo* behaviour. A further purpose was to extend the knowledge about the requirements for bioactivity, including the effect of alumina additions.

* *Present address*: Institute of Optics and Electronics, Academia Sinica, PO Box 355, Chengdu, Sichuan, People's Republic of China.

0957–4530/90 $03.00 + .12 © *1990 Chapman and Hall Ltd.*

TABLE I Correlation matrix for the glass compositions

	Na_2O	CaO	P_2O_5	B_2O_3	Al_2O_3
Na_2O	1.000	0.047	0.026	−0.040	−0.051
CaO	0.047	1.000	−0.016	0.033	0.071
P_2O_5	0.026	−0.016	1.000	−0.077	−0.009
B_2O_3	−0.040	0.033	−0.077	1.000	−0.040
Al_2O_3	−0.051	0.071	−0.009	−0.040	1.000

2. Materials and methods

The glass compositions were chosen to provide a basis for statistical evaluation. The correlation matrix is shown in Table I. All coefficients are much less than 0.1 and, hence, cross-correlation may be avoided. The glass compositions are shown in Table II. The raw materials used were SiO_2, Na_2CO_3, $CaCO_3$, $CaHPO_4 \cdot 2H_2O$, Al_2O_3 and H_3BO_3. The glasses were melted in a platinum crucible for 2 to 3 h at 1340 to 1410° C and cast into a preheated graphite mould. Conical implants with a length of 5 mm, a base diameter of 2.5 mm and a top angle of 9° were obtained.

The durability of the glasses was determined gravimetrically *in vitro*. The annealed glasses were crushed and sieved to a grain fraction of 297 to 500 μm. Before testing, the glasses were washed in deionized water, rinsed in ethanol and rapidly dried. For each glass, four samples of 200 mg grains were immersed in a Tris buffer solution at 36.5 ± 0.5°C. The Tris solution, with an initial pH of about 7.3, contained 50 mM Tris(hydroxylmethyl)aminomethane and 45 mM HCl.

Six cones of each glass were implanted in rabbit tibia, the tip of the cones pointing to the marrow. The bone preparation was done under sterile conditions using a burr for dental implants (Frialit®) at approximately 700 r.p.m. under irrigation with 0.9% NaCl solution. Before implantation the glasses were washed and sterilized ultrasonically in ethanol. The rabbits used were 4 to 7 months old with a weight of 4 to 5.5 kg. After 8 weeks they were killed. The specimens were fixed in buffered formaldehyde and embedded in methylmethacrylate. Histological sections 6 to 10 μm thick were prepared using the cutting–grinding technique [7]. After preparation of the histological sections, the remaining blocks were studied using scanning electron microscopy (SEM) and energy-dispersive X-ray analysis (EDXA). The compositional profiles across the interface provide information on the *in vivo* corrosion. Each profile is based on 8 to 10 normalized spot analyses. One difficulty in this study

TABLE II Glass compositions by synthesis (wt %)

Glass	Designation	Na_2O	CaO	P_2O_5	B_2O_3	Al_2O_3	SiO_2
1	S63.5P6	15.00	14.00	6.00	0.50	1.00	63.50
2	S57.5P5	16.00	18.00	5.00	3.00	0.50	57.50
3	S65.5P1	17.00	13.00	1.00	1.00	2.50	65.50
4	S52P3	18.00	24.00	3.00	0.00	3.00	52.00
5	S56P6	19.00	16.00	6.00	1.50	1.50	56.00
6	S51P7	20.00	17.00	7.00	3.00	2.00	51.00
7	S51P2	21.00	21.00	2.00	2.00	3.00	51.00
8	S64P0	22.00	10.00	0.00	2.50	1.50	64.00
9	S53P4	23.00	20.00	4.00	0.00	0.00	53.00
10	S45P7	24.00	22.00	7.00	2.00	0.00	45.00
11	S52P8	25.00	12.00	8.00	0.50	2.50	52.00
12	S46P0	26.00	25.00	0.00	2.00	1.00	46.00
13	S38P8	27.00	23.00	8.00	1.00	3.00	38.00
14	S48P2	28.00	19.00	2.00	1.50	1.50	48.00
15	S55.5P4	29.00	11.00	4.00	0.00	0.50	55.50
16	S45.5P5	30.00	15.00	5.00	2.50	2.00	45.50

was to section the cones along their axis. At the mantel surface of the cone the thickness of the silica-rich and the calcium phosphate-rich layers appears thicker the further away from its axis the cone is sectioned. Thus, the compositional profiles obtained can be interpreted only qualitatively. Caution is also needed in interpreting the compositional changes over very short distances, since the layers might not be perfectly aligned with the beam. This can result in an erroneous analysis.

3. Results and discussion

3.1. *In vitro* solubility

The weight loss during immersion for 6 and 24 h in Tris buffer solution is shown in Table III. The solubility varies considerably among the compositions studied. Thus, large differences in the tissue response are expected. Generally it can be concluded that the solubility increases with higher soda content and decreases with higher silica and alumina contents.

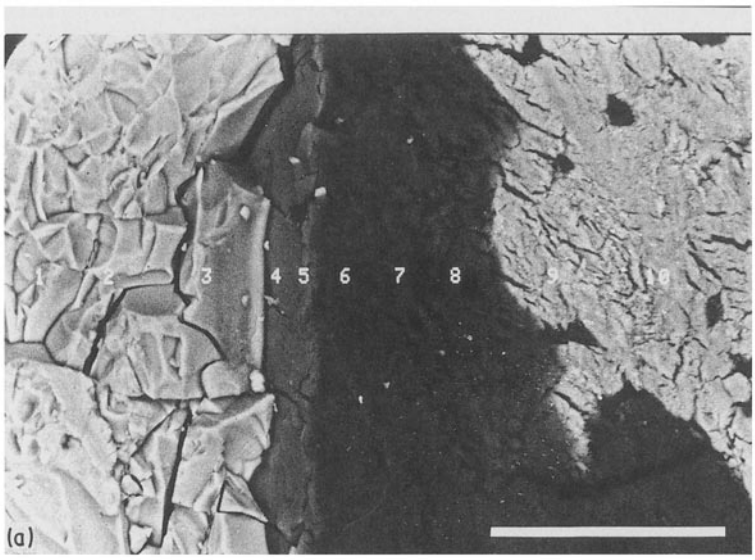
3.2. *In vivo* behaviour

The glasses in this investigation show a broad spectrum of physical and biomedical properties, ranging from almost inert glasses without bone contact to rather soluble glasses which bond to bone. An attempt to quantify the tissue response histologically by planimetric determination was made. However, the scatter in the results was too large to allow a statistical evaluation. The reason for this may be differences in the initial contact between implant and bone or differences in the initial fixation of the implants. Thus, the glass–tissue interfaces were studied using SEM

TABLE III Weight loss ($mg\,g^{-1}$ glass) during 6 and 24 h immersion in Tris buffer solution at 36.5 ± 0.5° C (average of four samples)

Glass	Weight loss 6 h ($mg\,g^{-1}$)	Weight loss 24 h ($mg\,g^{-1}$)	Glass	Weight loss 6 h ($mg\,g^{-1}$)	Weight loss 24 h ($mg\,g^{-1}$)
1	3.5 ± 0.9	6.8 ± 0.3	9	28.4 ± 3.7	58.6 ± 3.4
2	9.3 ± 0.9	32.4 ± 1.0	10	25.7 ± 1.1	53.1 ± 2.8
3	4.2 ± 0.3*	4.4 ± 0.8	11	13.6 ± 2.4	35.8 ± 1.6
4	5.3 ± 0.8*	21.8 ± 1.4	12	46.0 ± 1.8	85.7 ± 7.1
5	7.7 ± 1.0	22.2 ± 0.8	13	36.0 ± 3.4	47.3 ± 1.9
6	21.2 ± 1.2	41.4 ± 1.9	14	36.4 ± 0.7*	69.7 ± 3.2
7	14.8 ± 0.6	29.5 ± 1.0	15	30.1 ± 4.1	62.0 ± 2.9
8	nd	1.8 ± 0.3	16	33.5 ± 0.8*	59.3 ± 2.5

nd, not detectable; *only three samples.



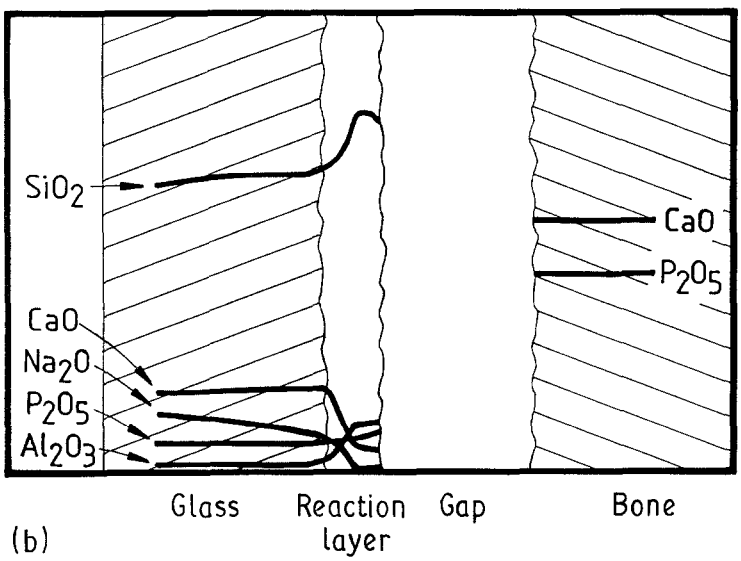


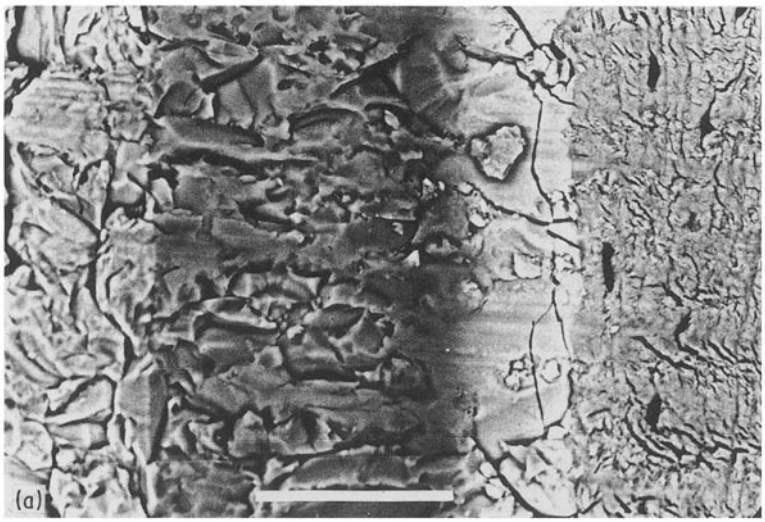
Figure 1 (a) SEM image of glass 1, showing no contact after 8 weeks in rabbit tibia. Bar = 50 μm. (b) Corresponding compositional profiles across the interface.

and EDXA. In Figs 1 to 6 the most interesting glasses and the corresponding compositional profiles across the interface are shown.

Glasses 1, 3 and 8 were found to be almost inert. Consequently, they do not bond to bone. The bone contact is also poor. The low solubility (Table III) is mainly due to high silica contents in combination with Al_2O_3 addition. A thin silica-rich layer develops but no calcium phosphate formation occurs at the surface. Fig. 1 shows an SEM image of the glass–bone interface of glass 1. The corresponding compositional profiles show that the P_2O_5 content is fairly constant throughout the glass, whereas sodium and calcium are leached.

In contrast to the glasses of low solubility, the rather soluble glasses 9, 10, 12, 14 and 15 bond to bone. Glasses 9, 10, 14 and 15 show typical behaviour of bioactive glass exhibiting silica-rich and calcium phosphate-rich layers (compare glass 15, Fig. 2). It can be noted that the alumina content of 1.5 wt % in glass 14 is tolerated without loss of bioactivity. Glass 12 does not contain phosphate. Nevertheless a thick silica-rich layer forms and in some areas calcium and phosphorus accumulation occurs. Thus, phosphate from the solution migrates into the silica-gel. The calcium- and phosphorus-rich layer is, however, non-uniform and over fairly large areas no accumulation of calcium and phosphorus was observed. In these areas the calcium- and phosphorus-rich layer could have been too thin to be detectable. The bone-bonding of glasses 12 and 15 was previously established by a push-out test [8].

Glasses 2, 4, 5, 6, 7, 11, 13 and 16 do not bond to bone, although they undergo extensive reactions. Thus, in their *in vivo* behaviour these glasses fall between the nearly inert and the bioactive ones. Glass 2 shows formation of a silica-rich layer, but calcium phosphate formation at only one spot corresponding to about 15% of the glass–cortex interface line. The bone contact is good but no bonding is observed. According to Ogino *et al.* [9], for a glass in the SiO_2–Na_2O–CaO–P_2O_5 system to develop a calcium- and phosphorus-rich surface layer, the SiO_2 content must not exceed 60 mol %. Since B_2O_3 and Al_2O_3 are included in glass 2, it cannot be compared directly with the work by Ogino *et al.* However, considering the solubility-reducing effect of Al_2O_3 and the SiO_2 content of 57.5 wt % (59.1 mol %), this glass is not expected to develop a calcium phosphate layer. Therefore, the appearance of calcium phosphate at



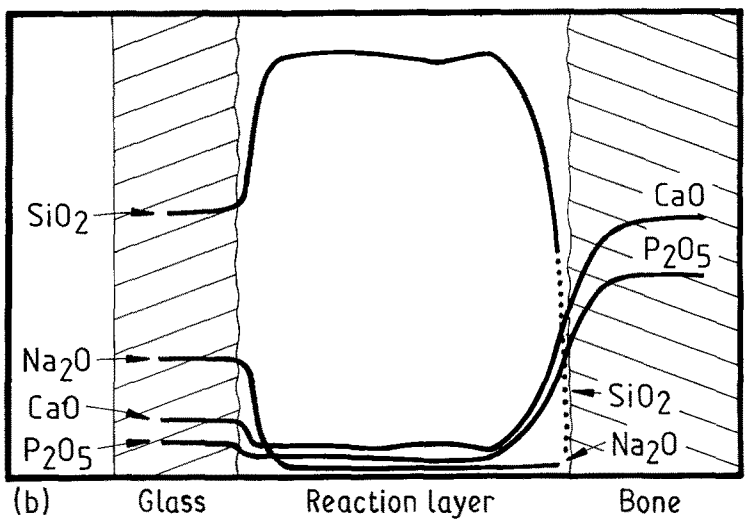


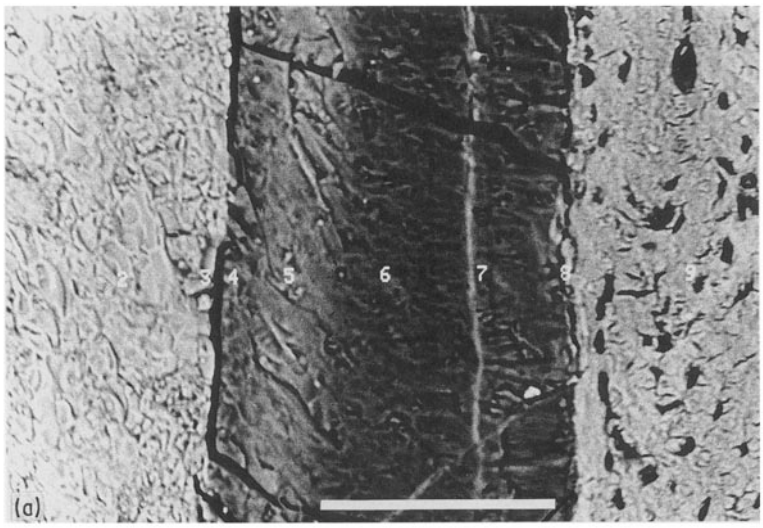
Figure 2 (a) SEM image of glass 15, showing bonding after 8 weeks in rabbit tibia. Bar = 50 μm. (b) Corresponding compositional profiles across the interface.

one spot could be due to an inhomogeneity in the glass. Glass 4 (Fig. 3) and glass 6 exhibit fairly thick silica-rich layers, but there are no signs of calcium phosphate formation at the surface. Bone seems to be only in contact with these glasses, not bonded to them. In both glasses Al_2O_3 is enriched in the reaction layer.

In glass 7 (Fig. 4) and glass 13 (Fig. 5) a limited accumulation of calcium and phosphorus occurs. For glass 7 the bone contact is good but the glass does not bond to the bone. There is, apart from an alumina enrichment, also accumulation of calcium and phosphorus in the outer part of the silica layer (Fig. 4b). However, the silica content remains high. The reaction layer is non-uniform and in some areas the bone is in direct contact with the silica-rich surface (Fig. 4c). For glass 13 the bone contact is poor. The compositional profiles across the interface (Fig. 5) are quite different from those in the other glasses. The glass is depleted of sodium to a considerable depth but the calcium and phosphorus contents are high. The phosphorus content is considerably higher throughout the sodium-depleted layer than in the bulk glass. If the discontinuity in the compositional profiles in the middle of the sodium-depleted layer is not considered, the calcium-to-phosphorus ratio is between 1.53 and 1.65 throughout this layer. Similar ratios are observed in the calcium- and phosphorus-rich layer in typical bioactive glasses (e.g. glass 15). This suggests that the calcium phosphate formed within the reaction layer in this glass is the same as that frequently observed in bioactive glasses. Thus, only the extent of calcium and phosphorus accumulation is limited. The lack of bonding for glasses 7 and 13 is probably caused by a bone-bonding incompatibility of the silica- and alumina-containing surface.

Glasses 5, 11 and 16 show formation of a calcium- and phosphorus-rich surface layer. However, bone-bonding is poor or absent. Glass 5 (Fig. 6) shows good bone contact but poor bonding. This could be a consequence of the high SiO_2 content and the Al_2O_3 addition, which gives a less soluble glass. It is possible that this glass would bond if the implantation time was extended. It should be noted that the Al_2O_3 content of 2 wt % in glass 16 and 2.5 wt % in glass 11 do not limit the accumulation of calcium and phosphorus within the silica-rich layer. The lack of bonding for these two glasses could be due to adsorption of Al^{3+} on the calcium- and phosphorus-rich surface.

Table IV summarizes the *in vivo* reactions, i.e. formation of silica-rich layer, formation of calcium- and phosphorus-rich layer, and bone response. In the table the Al_2O_3 content is also included. The glasses may be



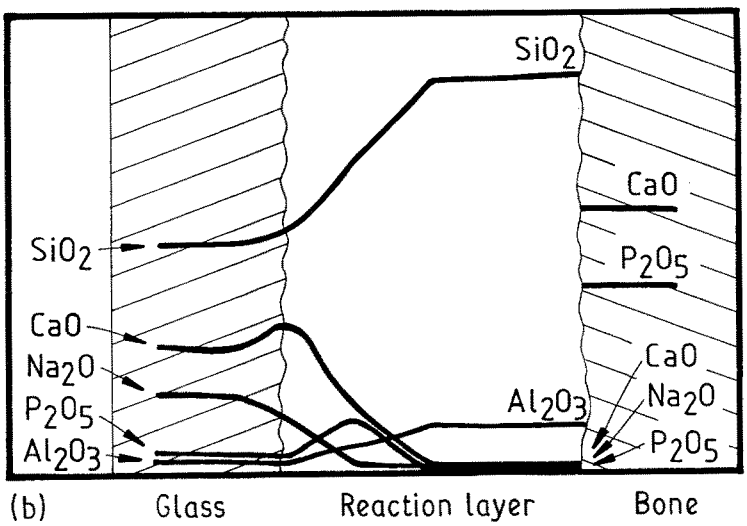


Figure 3 (a) SEM image of glass 4, showing contact after 8 weeks in rabbit tibia. Bar = 100 μm. (b) Corresponding compositional profiles across the interface.

divided into groups depending on their behaviour. The classification is based on the assumption that if the silica-gel cannot bind calcium phosphate, then it also cannot bond to bone. The groups are as follows.

TABLE IV Summary of the *in vivo* behaviour. The Al_2O_3-content is included

Glass	Silica layer	Calcium and phosphorus layer	Bone response	Al_2O_3 content (wt %)	Group
1	Thin	No	No contact	1.0	A
2	Yes	No*	Contact	0.5	B, (D)
3	Thin	No	No contact	2.5	A
4	Yes†	No	Contact	3.0	B
5	Yes	Yes	Contact	1.5	D, (E)
6	Yes†	No	Contact	2.0	B
7	Yes†	Limited	Contact	3.0	(B), C
8	Thin	No	Poor contact	1.5	A
9	Yes	Yes	Bonding	0.0	E
10	Yes	Yes	Bonding	0.0	E
11	Yes	Yes	Poor contact	2.5	D
12	Yes	Yes	Bonding	1.0	E
13	No‡	Limited	Poor contact	3.0	C
14	Yes	Yes	Bonding	1.5	E
15	Yes	Yes	Bonding	0.5	E
16	Yes	Yes	Poor contact	2.0	D

*Calcium and phosphorus layer at one spot (15% of the interface).
†Al_2O_3 enrichment.
‡Sodium depletion.

A. Nearly inert glasses. Only small changes in the surface composition and hardly any bone contact.

B. Fairly high solubility. Bone contact but no bonding. Formation of a silica-rich layer but no accumulation of calcium and phosphorus. This is apparently due to too high a stability of the silica-rich layer. The high stability is caused either by a high silica content or by Al_2O_3 enrichment in the surface.

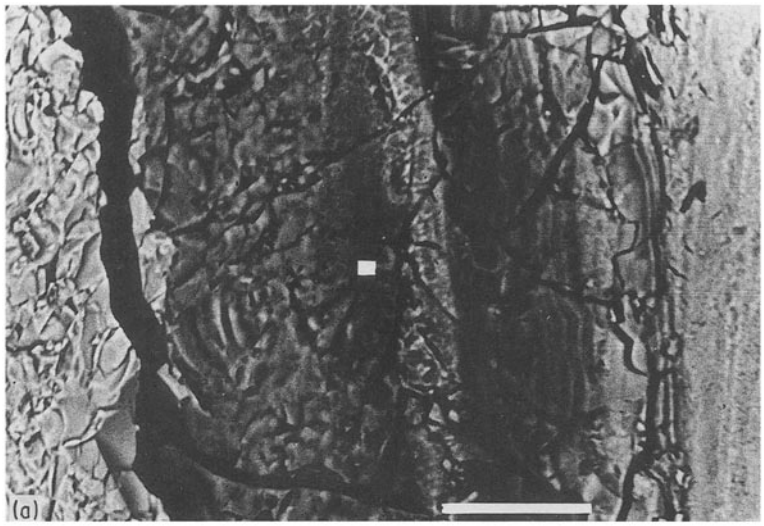
C. Fairly high solubility. Bone contact but no bonding. Formation of a silica-rich (or sodium-depleted) layer. Limited accumulation of calcium and phosphorus, due to stabilization of the silica structure. In the investigated glasses the stabilization was due to Al_2O_3. The lack of bonding is probably due to a bone-bonding incompatibility of the silicon- and aluminium-containing calcium phosphate surface.

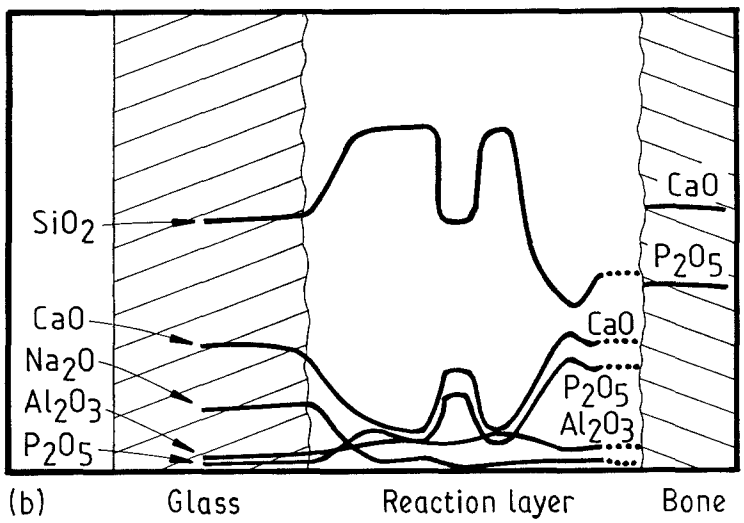
D. Fairly high solubility formation of a calcium- and phosphorus-rich surface layer, but no bone-bonding. The lack of bonding could be due to aluminium release into the tissue or to adsorption of Al^{3+} on the calcium- and phosphorus-rich surface layer.

E. Bioactive glasses. Formation of a calcium- and phosphorus-rich surface layer and bone-bonding.

3.3. Phenomenological description

By assigning numerical values to the groups A to E it is possible to develop a phenomenological model. The





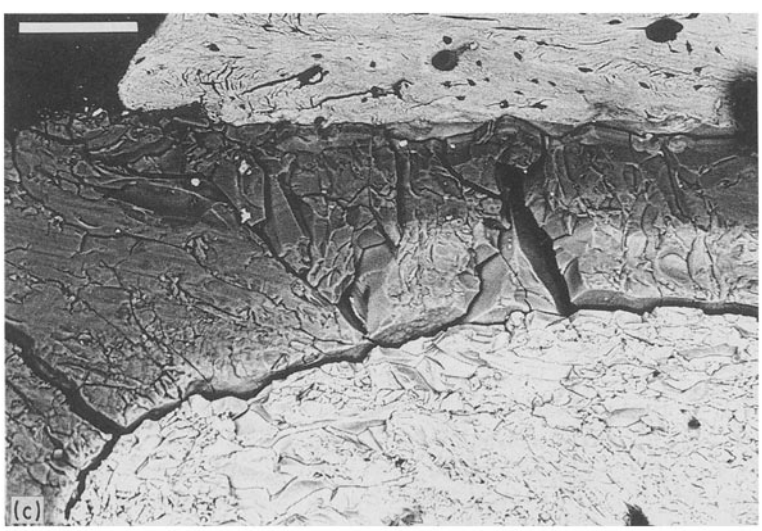
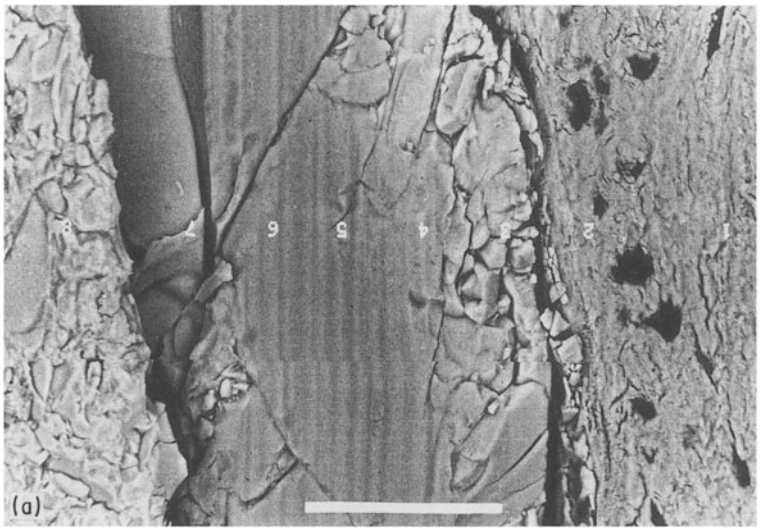


Figure 4 (a) SEM image of glass 7, showing contact after 8 weeks in rabbit tibia. Bar = 50 μm. In this area a limited accumulation of calcium and phosphorus has occurred. (b) Corresponding compositional profiles across the interface. (c) Area showing good contact but no calcium- and phosphorus-rich layer. Bar = 100 μm.

assignations are A = 1, B = 2, C = 3, D = 4 and E = 6. Thus for a glass to be bioactive it should have a number above about 5, with composition in wt %:

$$\text{Reaction number} = 88.3875$$
$$- 0.011\ 6272[SiO_2]^2$$
$$- 0.980\ 188[Na_2O] - 1.123\ 06[CaO]$$
$$- 1.205\ 56[P_2O_5] - 0.560\ 527[B_2O_3]^2$$
$$- 2.086\ 89[Al_2O_3]$$
$$R^2 = 97.25\% \qquad \sigma = 0.42$$

When developing the model, numerical values corresponding to the classification in Table IV were used. For glass 7 the calcium- and phosphorus-rich layer is



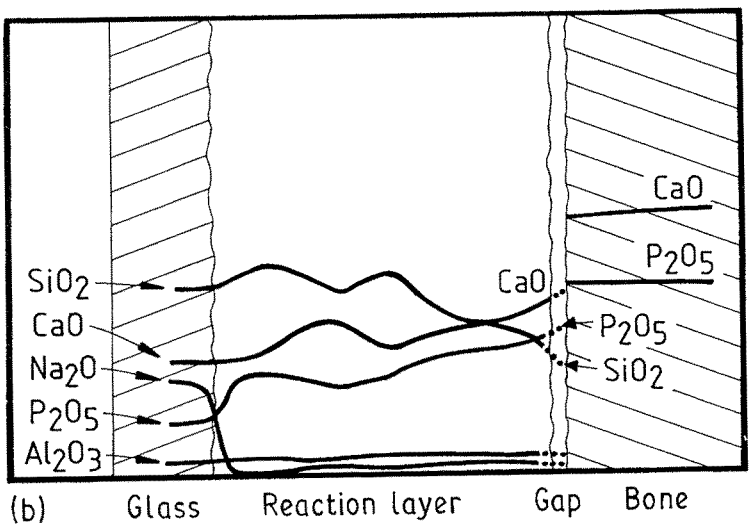


Figure 5 (a) SEM image of glass 13, showing poor contact after 8 weeks in rabbit tibia. Bar = 50 μm. (b) Corresponding compositional profiles across the interface.

non-uniform. However, it is extensive enough for the glass to be classified as being type C. For glasses 2 and 5 the classification is more difficult. Glass 2 shows calcium phosphate formation at one spot, which corresponds to about 15% of the bone–glass interface. This is assumed to be due to an inhomogeneity in the glass. Thus, the glass is considered to be of type B. For glass 5 (Fig. 6) bone-bonding could exist at a few spots. However, most of the surface seems only to be in contact with the bone and the formation of new bone seems to be disturbed. Therefore, glass 5 is considered to be of type D. If glasses 2 and 5 are classified as type D and E, respectively, instead of type B and D, the regression coefficient is only 91.33%.

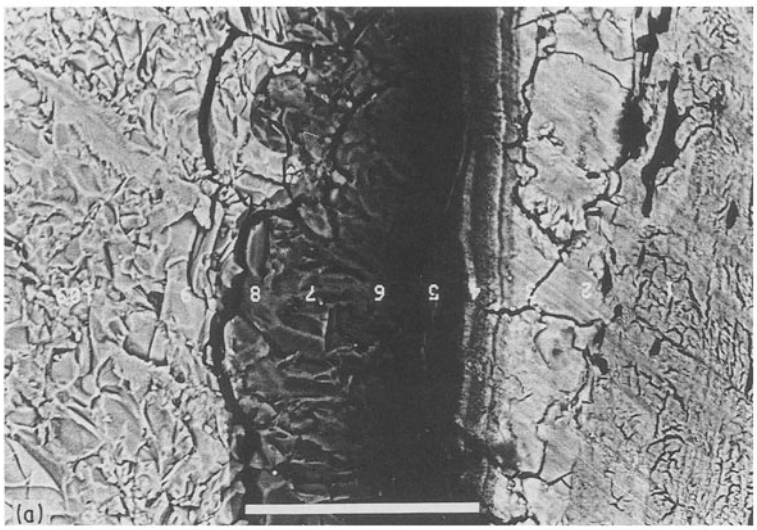
Although the dependent variable is discretized, the model can be used for estimations of the tissue response, because none of the terms in the polynomial gives rise to oscillating behaviour. As an example, the model can be tested on Hench's 45S5 Bioglass®. The composition of this glass is (in wt %): SiO_2, 45.0; Na_2O, 24.5; CaO, 24.5; and P_2O_5, 6.0. The model gives a numerical value of 6.08. By addition of 1 wt % Al_2O_3 the value decreases to 5.03. An Al_2O_3 addition of 1.5 wt % decreases the value to 4.51. Thus, the calculation suggests that the bioactivity might be lost at Al_2O_3 additions exceeding 1 to 1.5 wt %.

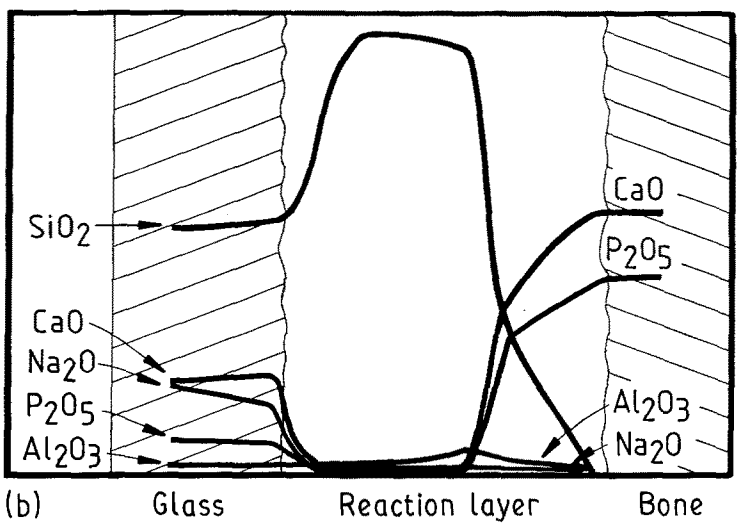
3.4. Composition effects

Glasses 1, 3 and 8 show low solubility and the bone contact is poor. For the more soluble glasses 4 and 6 the bone contact is good, although no bonding occurs. No accumulation of calcium and phosphorus occurs at the surface of any of these glasses. The surface structures formed on glasses 4 and 6 have a higher silica content, i.e. a more flexible and hydrated structure, than glasses 1, 3 and 8. Therefore, it is suggested that the formation of a silica-rich gel results in good biocompatibility, although no bonding occurs. Also, the higher dissolution of ions from glasses 4 and 6 might stimulate the bone growth.

For glass 1 (Fig. 1) it can be seen that the Al_2O_3 content increases considerably near the surface. In SiO_2–Na_2O–CaO–P_2O_5 glasses of this high silica content no calcium or phosphorus accumulation occurs [9]. Thus, for Al^{3+} ions to bond to the silica structure, this does not need to be as flexible as for the formation of calcium phosphate.

For glass 5 the bonding is poor or non-existent. The Al_2O_3 content in this glass is 1.5 wt %. From Fig. 6b it can be seen that a slight Al_2O_3 enrichment occurs in the silica-rich layer. However, the Al_2O_3 content decreases closer to the implant surface, where the accumulation of calcium and phosphorus occurs.





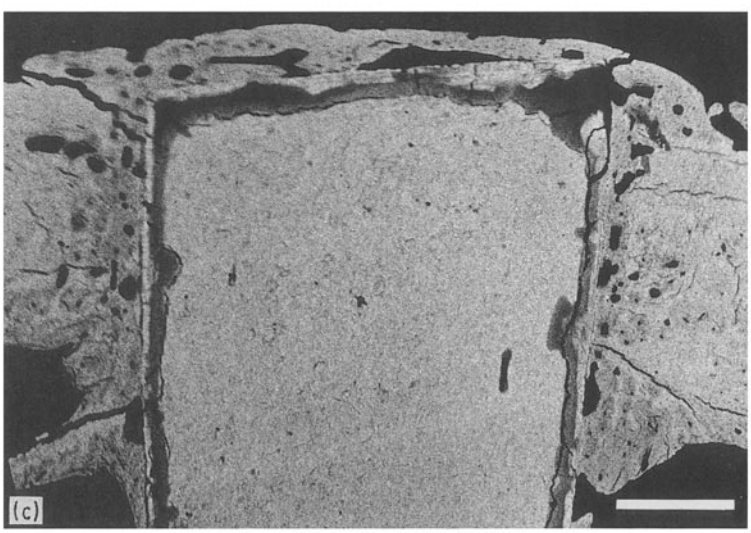


Figure 6 (a) SEM image of glass 5 after 8 weeks in rabbit tibia. Bar = 100 μm. (b) Corresponding compositional profiles across the interface. (c) Overview of glass 5 in the tibia. Bone-bonding might exist in some areas, but most of the glass surface seems to be only in contact with the bone. Bar = 0.5 mm.

Thus, the Al_2O_3 content is not sufficient to stabilize the silica structure sufficiently to prevent calcium phosphate build-up. Glass 4 shows a different behaviour. From Fig. 3b it can be seen that whereas the silica content in the silica-rich layer is about 80% higher than in the bulk glass, the alumina content in the silica-rich layer is about five times as high as in the bulk glass. Thus, alumina is enriched in the silica-rich layer. It has recently been shown that the calcium phosphate build-up could result from complexation of phosphate by the silica-gel [8]. It has been suggested that the Al_2O_3 enrichment is due to a preferential formation of silica–aluminium chelates instead of phosphorus–silicate complexes [8, 10]. This suggestion is supported by the fact that no accumulation of calcium phosphate occurs in the silica-rich layer of glass 4, whereas aluminium is enriched. The behaviour of glass 6 is almost identical to that of glass 4. Thus, in

these glasses the Al_2O_3 stabilizes the silica structure sufficiently to inhibit calcium phosphate build-up. The Al_2O_3 enrichment apparently has tied up the silica-gel and reduced its flexibility so that no calcium phosphate build-up occurs. It could also be that the Al_2O_3 content is sufficiently high to occupy the sites where calcium phosphate formation could have taken place.

For glass 7, which contains 3 wt % Al_2O_3, calcium and phosphorus accumulation occurs within the silica-rich layer (Fig. 4b). However, the calcium and phosphorus contents do not exceed the silica content. Thus, the accumulation of calcium and phosphorus is limited. This suggests that in glass 4, which is less soluble than glass 7, the alumina stabilizes the silica structure sufficiently to prevent calcium phosphate formation within it. In the more soluble glass 7 the alumina only stabilizes the structure to some extent. A certain flexibility of the silica structure and a sufficient number of non-bridging oxygens still exist. Thus, in glass 7 a limited calcium phosphate formation takes place.

Glass 13 shows a similar behaviour. A limited accumulation of calcium and phosphorus takes place in the reaction layer. As in glass 7, the silica content remains high. However, some caution must be used in interpreting the results for glass 13, since its overall structure may differ from that in glasses of higher silica content. It might even be that a silicon-rich droplet phase has formed and that the matrix is a phosphate glass.

4. Conclusions

Neither the bone contact nor the bonding could be satisfactorily quantified histologically. Therefore, the evaluation of the tissue response was based on the SEM–EDXA study. A correlation between the corrosion reactions within the glass and the tissue response was obtained. It was also possible to develop a phenomenological model that describes the *in vivo* behaviour as a function of the glass composition.

On the basis of the results obtained, some conclusions can be drawn regarding the compositional dependence of the bioactivity, the effect of alumina additions and the requirements for calcium phosphate accumulation in the silica-gel.

1. The present results support the previous conclusion that the calcium phosphate build-up occurs within the silica-gel, not on top of it [8]. The silica-gel must be sufficiently hydrated and flexible to allow calcium phosphate build-up.

2. For some glasses a thick silica-rich surface layer forms and the bone contact is good, but no bonding occurs. It is suggested that the formation of a silica-rich gel results in good biocompatibility. Also, the high release of ions might stimulate the bone growth.

3. The results suggest that alumina addition to the glass may inhibit the bone bonding in different ways.

(a) By considerably decreasing the solubility so that no silica-rich layer forms.

(b) By stabilizing the silica-gel in glasses of higher solubility. This may be interpreted as formation of aluminium–silicate chelates instead of phosphorus–silicate complexes. Depending on the silica content and the alumina addition, the accumulation of calcium and phosphorus is inhibited, limited or not significantly affected.

(c) For glasses which exhibit a calcium- and phosphorus-rich layer, the bone bonding could be inhibited by adsorption of Al^{3+} on the calcium- and phosphorus-rich surface. Release of aluminium into the tissue might also contribute to the lack of bonding.

It can be pointed out that although a calcium phosphate layer forms, the glass may in some cases show only bone contact, not bonding. Thus, the formation of a calcium phosphate-rich layer at the glass surface cannot be taken as a sign of bioactivity in glasses containing components such as Al_2O_3.

References

1. L. L. HENCH, R. J. SPLINTER, W. C. ALLEN and T. K. GREENLEE, *J. Biomed. Mater. Res. Symp.* **2** (1971) 117.
2. L. L. HENCH, *Adv. Ceram. Mater.* **1** (1986) 306.
3. U. GROSS and V. STRUNZ, *J. Biomed. Mater. Res.* **19** (1985) 251.
4. *Idem, ibid.* **14** (1980) 607.
5. Ö. H. ANDERSSON, K. H. KARLSSON, K. KANGASNIEMI and A. YLI-URPO, *Glastech. Ber.* **61** (1988) 300.
6. A. A. APPEN, Steklo i keram. **10** (1953) 7.
7. K. DONATH, Der Präparator **34** (1988) 197.
8. Ö. H. ANDERSSON, K. H. KARLSSON and K. KANGASNIEMI, *J. Non-Cryst. Solids* accepted.
9. M. OGINO, F. OHUCHI and L. L. HENCH, *J. Biomed. Mater. Res.* **14** (1980) 55.
10. K. H. KARLSSON, K. FRÖBERG and T. RINGBOM, *J. Non-Cryst. Solids* **112** (1989) 69.

Received 20 February
and accepted 1 March 1990