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The incorporation of hydroxyapatite into glass-polyalkenoate ("glass-ionomer") cements: a preliminary study

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The effect of adding finely divided hydroxyapatite (HAp) powder to glass-polyalkenoate cements has been studied. Two different glasses were used in cement formation, an oxide and a fluoride glass. Cements were prepared at a powder:liquid ratio of 2:1, higher ratios being unattainable because of the low bulk density (hence large volume fraction per unit mass) of HAp powder. For the oxide glass there was a steady reduction in compressive strength and an increase in working and setting times with increased loadings of HAp. By contrast, for the fluoride glass, there was a plateau region from 2.5 to 40% by mass HAp in the glass powder in which the compressive strengths and the working and setting times remained approximately constant. At HAp levels above 40%, as for the oxide glass, there was a significant reduction in strength and an increase in working and setting times. The presence of HAp in the cement was not found to inhibit the development of compressive strength with time for cements prepared from the fluoride-containing glass. Cements prepared from the oxide glass, by contrast, did not increase in strength with time and this feature was also not changed by the presence of HAp.

1. Introduction

Glass-polyalkenoate cements are a family of materials widely used in clinical dentistry [1]. They are also being developed for other clinical uses, such as building up the alveolar ridge of edentulous patients [2] and as cements for the fixation of joint prostheses in orthopaedic surgery [3–5].

Glass-polyalkenoates comprise powdered glass which is reacted with a polycarboxylic acid such as poly(acrylic acid) or acrylic/itaconic acid copolymers, in the presence of water [1]. The resulting setting reaction is an acid/base reaction which generates a polysalt. This is the initial matrix. Subsequently post-hardening maturation processes take place which result in the formation of a silicon-containing phase [6]. This phase has been assumed to be a kind of amorphous hydrated silicate [7].

Glass-polyalkenoates are known to show generally good biocompatibility, including in bone-contacting applications [8]. Among the factors that contribute to this are the fact that these cements release ions such as Ca^{2+}, PO_4^{3-} and F^-. The former are the main constituents of the mineral hydroxyapatite, which itself is the major component of teeth and bones. Fluoride, in appropriate doses, promotes bone growth and retards carries development in teeth [9]. It does so by exchanging with hydroxyl ions in hydroxyapatite to form the mineral phase apatite (sometimes called fluoroapatite) [10]. Apatite, in addition to its increased resistance to attack by plaque acids in the mouth, has a lower crystal energy than hydroxyapatite (HAp). It is more thermodynamically favoured than HAp, hence it does not spontaneously revert to hydroxyapatite [10]. Recently, it has been shown that the glasses used in these cements will crystallize to, *inter alia*, apatite if held above the glass-transition temperature for a prolonged period [11]. Thus, it seems clear that in the glasses, at least, there is a possibility of readily forming the highly biocompatible mineral apatite. This, it has been suggested, is part of the cause of the excellent biocompatibility of the cements made from these glasses [11].

Despite the many attractive features of glass-polyalkenoates, they do suffer from disadvantages, including brittleness and poor wear characteristics. A number of different fillers have been used to attempt to overcome these problems. These include silver-cermets [12], which are the basis of a successful and widely used restorative material [13], and also stainless-steel powders [14] and carbon and alumino-silicate fibres [15]. The wear characteristics in clinical service of the silver-cermet glass-polyalkenoates have been found to be an improvement over the unfilled material [13]. In the case of the experimental fillers, cements were also found to have improved physical properties; stainless-steel powder gave cements of improved tensile and compressive strengths [14], while fibre reinforcement led to higher Young's modulus and increased flexural strength [15]. Thus fillers are being widely used in the development of glass-polyalkenoate cements with improved properties.

Finely divided hydroxyapatite has been used as a filler in a number of biomaterials, though not previously in glass-polyalkenoates. It has been found to improve the physical properties of novel bone cements based on either ethyl/butyl methacrylate co-polymers [16] or 4-methacryloyloxy ethyl methacrylate/methyl methacrylate co-polymers [17]. It has also been included in zinc polycarboxylate cements [18] to improve their biocompatibility. These latter formulations are now commercially available as dental cements of enhanced biocompatibility.

In view of the improvements found in the physical properties of filled glass-polyalkenoates cements, it is of interest to study the effect of including hydroxyapatite as the filler for these cements. Glass-polyalkenoates have been found to interact with HAp via the carboxylate groups in the polymer, an interaction claimed to be responsible for the adhesion of glass-polyalkenoates to teeth [19]. In other studies, the adsorption of carboxylic acids onto HAp has been studied, and a distinct interaction between such acids and HAp found [20]. Polymers bearing such functional groups have also been found to interact with HAp [21]. Hence, using HAp as the filler for glass-polyalkenoates cements may result in materials which not only have improved biocompatibility, but which also possess potentially interesting mechanical properties. The particular properties examined have been setting time and compressive strength, including the change in strength with time. The variation in setting time and compressive strength with increasing mass fractions of HAp has been studied in detail in the current work, and at one level of HAp (i.e. 10%) the influence on the development of strength with ageing has been determined. Two different glasses were used, an oxide and a fluoride glass, both in conjunction with a 40% aqueous solution of homopolymer poly(acrylic acid). The results are reported below.

2. Materials and methods

Two glasses were used in this study, designated MP4 (from Cookson plc) and G200D (prepared at the Laboratory of the Government Chemist, UK–LGC). The composition of the glasses is shown in Table I. In each case, the glasses were ground to pass through a 45 µm sieve.

Hydroxyapatite (Bio-Gel HTP, from Bio-Rad Laboratories, Richmond, California, USA) was mixed into the glass component using a mill mixer at various percentages: (a) at 2.5, 5.0, 10.0 20.0 and 25.0% for the glass MP4; and (b) at 2.5, 5.0, 10.0, 20.0, 25.0, 30.0, 40.0 and 50.0% for the glass G200D.

TABLE I Composition of the glasses

MP4		G200D	
Al_2O_3	35%	Al_2O_3	16.6%
SiO_2	28%	SiO_2	29.0%
CaO	26%	Na_3AlF_6	5.0%
Na_2O	11%	CaF_2	34.3%
		AlF_3	5.3%
		$AlPO_4$	9.9%

Poly(acrylic acid) (Versicol E7, from Allied Colloids, Low Moor, Bradford, UK) in 40% aqueous solution was used in the preparation of cements. Cements were made by spatulation of the glass powder into the aqueous polymer solution at a powder/liquid ratio of 2:1.

Working and setting times were obtained at 23 °C using an oscillating (Wilson) rheometer [22]. This device comprises a pair of grooved metal plates between which the cement is placed immediately mixing is complete. The upper plate is oscillated with respect to the lower plate by applying a continuous reciprocating force to the spring. As the cement sets, so the degree of motion imparted to the upper plate by the spring decreases. The motion of the upper plate is plotted using a chart recorder and changes from extensive motion to little or no motion as the cement sets.

Compressive strength was determined for these cements, using 6 by 12 mm cylindrical specimens, which had been stored at 37 °C for 23 h. A universal testing machine (Instron 1185) was used at a cross-head speed of 1 mm min^{-1}. These procedures are as specified in the current British Standard for glass-polyalkenoate cements [23]. Where necessary, the statistical significance of the differences in results was examined using the Student's *t*-test.

For both glasses, the development of strength with time for the first month was studied using the cement formulation containing 10% HAp. Once again, the statistical significance of differences in results was examined using the Student's *t*-test.

3. Results and discussion

The effect of incorporating HAp into cements prepared from MP4 and G200D are shown in Tables II and III respectively.

Table II shows that, for MP4 glass, adding up to 2.5% HAp did not alter the compressive strength. Above 2.5%, increasing the percentage of hydroxyapatite caused a decrease in the compressive strength, and an increase in both the working and setting times.

TABLE II Effect on the mechanical properties of glass-polyalkenoate cements of adding hydroxyapatite to the glass component MP4

Hydroxy apatite (%)	Working time (min)	Setting time (min)	Compressive strength (MPa)[a]
0	2	9	20 (1)
2.5	3	19	20 (1)
5.0	6	34	18 (1)
10.0	10	55	14 (2)
20.0	10	76	11 (1)
25.0	–[b]	140	8 (1)

[a] The figures in parentheses indicate standard deviations.

[b] A very uneven trace, hence the working time could not be determined by oscillating rheometry.

TABLE III Effect on the mechanical properties of glass-polyalkenoate cements of adding hydroxyapatite to the glass component, G200D

Hydroxy apatite (%)	Working time (min)	Setting time (min)	Compressive strength (MPa)[a]
0	2	11	55 (8)
2.5	2	12	53 (4)
5.0	2	13	56 (5)
10.0	3	12	53 (7)
20.0	3	12	52 (3)
25.0	3	12	50 (6)
30.0	4	20	49 (7)
40.0	5	16	48 (3)
50.0	12	59	26 (2)

[a] The figures in parentheses indicate standard deviations.

At 20%, hydroxyapatite the strength had reached approximately half that of the parent cement containing no HAp. Furthermore, at increased loadings of HAp, the setting traces on the oscillating rheometer became less like the ideal "wine glass" shape, and more uneven. These changes were all significant at the 99% confidence level.

The results for G200D showed interesting differences from those for MP4. As can be seen from Table III, there was a slight decrease in strength, and a slight increase in working and setting times, when incorporating HAp at levels up to 40%. These changes in compressive strength were not statistically significant up to a loading of 40% HAp. However, the change between 40% and 50% HAp was significant at the 99% confidence level, so that at 50% HAp, the strength had dropped to less than half that of the parent cement. The working times and setting times were also considerably extended.

An attempt was made to form a cement using HAp alone as the powder, but without success. Previous results reported by Ellis *et al.* [21] had indicated that a reaction might occur, but this was found not to be the case, and the polymer/HAp mixtures were shown to be disintegrated in water due to the continued solubility of the polymer. Hence, it seems certain that in the cements HAp is not able to act as a co-reactant, but instead behaves simply as an unreactive filler. Thus the inclusion of HAp inhibits the reaction because it replaces a fraction of the reactive glass powder, thereby interfering with the acid–base setting process.

The two glasses responded differently to the inclusion of HAp. MP4 was more adversely affected; smaller amounts were required to extend to setting time to above an hour and to reduce the compressive strength to half of the value of the untreated cement. G200D, by contrast, required much larger quantities of HAp to increase the working time to about an hour and to reduce the compressive strength to half of the initial value. In addition, there was a plateau region in which considerable additions of HAp made no significant difference to the compressive strength, or to the working and setting times. The origin of these differences and of the plateau phenomenon for G200D is unclear, though similar effects have been observed previously with HAp-filled zinc polycarboxylate [18].

TABLE IV Effect of HAp on the development of strength with time

Glass	Compressive strength (MPa)[a]	
	One day	One month
G200D	55 (8)	60 (14)
G200D + HAp	53 (7)	62 (18)
MP4	20 (1)	17 (2)
MP4 + HAp	14 (2)	12 (1)

[a] The figures in parentheses indicate standard deviations.

Finally, the effect of HAp on the development of strength was studied using the formulations containing 10% HAp. The results for these experiments are shown in Table IV. From Table IV, it can be seen that the formulation based on G200 underwent a slight increase in strength with time, which was significant at the 95% level. By contrast, the formulation based on MP4 underwent a slight reduction in strength, though this was not statistically significant. In each case, the inclusion of 10% HAp into the cement did not alter the strength development behaviour. There was, however, an increase in standard deviation for the one-month-old cements prepared from G200D + 10% HAp. This increase in scatter may indicate that these particular cements become less homogeneous with time on storage in water.

4. Conclusions

This preliminary study has shown that the incorporation of hydroxyapatite into glass-polyalkenoate cements can be done only at low powder-to-liquid ratios, because of the high bulk density of HAp powder. The precise effect of incorporating hydroxyapatite has been found to depend on the type of glass. Cements prepared from the oxide-glass MP4 showed a significant reduction in properties with quite low percentage additions, i.e. 5–10%. By contrast, cements prepared from the fluoride glass, G200D, at the same percentages showed only a minimal loss of properties. Much larger amounts of HAp could be added to this glass before a significant decline became apparent in the resulting cements. HAp (at a level of 10%) was found to make no difference to the way in which strength developed, or failed to develop, as the cements were aged.

The overall effect of incorporating HAp is to slow down the setting reaction and to make the final cement weaker than equivalent cements without HAp. These changes may be beneficial for some of the proposed newer uses of glass-polyalkenoates such as in orthopaedic or maxillo-facial surgery. In particular, the reduction in the speed of set compared with those cements used in dentistry may have clinical advantages for such alternative applications. In addition, the presence of HAp in the fully set cements is likely to enhance their already good biocompatibility.

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