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The influence of hydroxyapatite: Zinc oxide ratio on the setting behavior and mechanical properties of polyalkenoate cements

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The influence of hydroxyapatite (HA) content on the setting behavior and mechanical properties of hydroxyapatite–zinc oxide–poly(acrylic acid) (HA–ZnO–PAA) composite cements were investigated as a function of HA content. The working time increased with HA content up to 45 wt % HA and then decreased whilst the setting time increased with increasing HA content. Mechanical properties were determined after storage in water at 37 °C for 1, 7 and 28 days. Young's moduli and compressive strength go through a maximum at approximately 30 and 45 wt % HA. Young's modulus increases with time, which is consistent with an ongoing crosslinking reaction.

1. Introduction

Despite their use in clinical practice over a period of 30 years, poly(methyl methacrylate) (PMMA) bone cements continue to present various problems with regard to biocompatibility and stability. New bioactive cements are required in order to reduce fibrous capsule formation at the bone-cement interface, thereby reducing the likelihood of aseptic loosening. Various strategies have been pursued, involving modification of acrylic bone cements, with additions of hydroxyapatite (HA) [1], bioactive glass and glass-ceramics [2] and bone particles [3]. The main aim of these investigations is to promote tissue integration and minimize fibrous capsule formation.

The presence of a fibrous layer between bone and the cement prevents the implant from being loaded properly. This interferes with the transfer of stress from the bone through the cement and implant to the bone beneath. Because of stress shielding, bone resorption is known to occur. Therefore, bone at the interface is often structurally very weak due to stress shielding or localized death of the bone and this invariably leads to loosening and clinical failure of the implant.

It is known that bioactive materials, which form a bond with bone, develop a surface that is different from the original surface before implantation. Fundamental studies and clinical applications have demonstrated that calcium phosphate biomaterials (HA ceramic, tricalcium phosphate and HA/tricalcium phosphate ceramic) are biocompatible and osteoconductive [4–6]. *In vivo*, these materials are non-toxic, antigenically inactive and bond directly to bone without any intervening connective tissue layer.

Eliminating the high set exotherm that accompanies a polymerization reaction would also be beneficial to the environment around the implant. Polyalkenoate cements formed from an acid-base reaction of poly(acrylic acid) (PAA) with glass particles, zinc oxide (ZnO) or apatites have potential as bone cements. PAA is a polyelectrolyte that has a simple structure and low toxicity [7]. It has the ability to complex calcium [8] and to form hydrogen bonds with proteins including collagen [9]. PAA will be used as the matrix in these composite cements. The main point to make about PAA is that it sets via a neutralization reaction, whereby the polyacid neutralizes a base (inorganic component within the cement) and sets at a temperature around that of the body. The surrounding bone will remain in a healthy state, where adhesion between it and the cement may be achieved.

It was reported that a PAA-based cement containing ZnO had a potential to be used in orthopedic applications [10]. However, although these cements are non-toxic, they were not bioactive and resulted in the formation of a fibrous collagen capsule layer. Blades *et al.* [11] compared the *in vivo* biological and biomechanical behavior of glass-ionomer cements to that of a conventional PMMA orthopedic cement. Aluminum, which is released from the setting glass-ionomer cement,

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was found to accumulate in regions of bone formation, both locally and at a distance from the implant material, inhibiting mineralization of osteoid.

In order to improve the bioactivity of the ZnO-based polyalkenoate cement and improve the mechanical properties, HA particles were introduced. The reasons for choosing HA include the ability to reinforce the polysalt matrix, increase Young's modulus as well as improving the materials bone bonding and bioactive properties.

In a previous study [12] we found that the PAA molar mass had a very significant effect on the fracture properties of a ZnO-HA-based cement. It is hoped that by varying the amounts of ZnO and HA in this system, a cement whose working and setting time can be manipulated, may be developed. Since the cement sets via an acid–base neutralization reaction, the surrounding bone will remain in a healthy state, where adhesion between it and the cement may be achieved.

This present paper investigates the influence of the HA content of the cement, on its setting behavior, whilst also relating the compressive strength and Young's modulus.

2. Experimental

2.1. Materials

Medical grade HA was obtained from Howmedica Stryker Osteonics (Raheen Industrial Estate, Dooradoyle, Limerick, Ireland).

A modified ZnO was supplied by Shofu (AHL) (Chiddingstone, Causeway, Tonbridge, Kent, UK). The PAA was obtained from CIBA specialty polymers (PO Box 38, Bradford, UK). They were designated E9 and E11 according to their molar mass characteristics. They were supplied as concentrated aqueous solution. The samples were freeze-dried, then ground and sieved below 90 μm prior to use.

2.2. Specimen fabrication

The powder mixtures consisting of varying amounts of apatite (by wt %) and varying amounts of ZnO (wt %) were prepared. Cements were then formed by thoroughly mixing the powder mixture with the PAA in a weight ratio of 3 : 1 and then mixing this with 10% m/m(+) tartaric acid solution in a weight ratio of 4.3 : 1. The cements have a PAA concentration of 60% m/m, cements with a concentration of 40% and 50% PAA were also produced. Cements were allowed to set in the appropriate mold for 1 h at 37 ± 2 °C then removed from the mold and stored in distilled water at 37 ± 2 °C prior to testing. All tests were carried out after 1, 7 and 28 days in water at 37 ± 2 °C.

2.3. Test methods

2.3.1. Compressive test

The compression tests were performed as described previously [12]. The testing procedure was based on the ISO standard "ISO 7489: 1986" Dental Glass Polyalkenoate Cements [13].

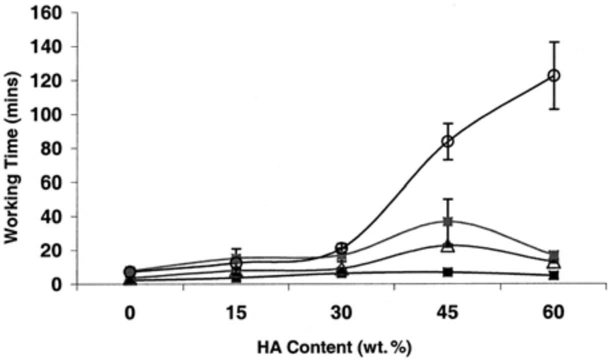

Figure 1 Working times for the E11/50% (-■-), E9/60 (-△-), 50(-■-) and 40% -○- cements.

2.3.2. The three point bend test

The test and method are based on ASTMS D790-1 [14]. The test method has been described previously [12]. Young's modulus is given by

$$E = \frac{PS^3}{4\delta bt^3}$$

where P is the load, S the span, δ the deflection at the center of the span, b the breath of the specimen and t its thickness. Young's modulus was calculated from the initial slope of the load–deflection plot.

2.3.3. Oscillating rheometry

Working and setting times were obtained at 24 °C using an oscillating (Wilson) rheometer [15] whose design and mode of operation has been described in detail elsewhere [16].

3. Results and discussion

The influence of the HA content of polyalkenoate cements on working and setting times are shown in Figs 1 and 2. Fig. 1 shows that as the HA content is raised the working time increases. This increase continues up to 45 wt % HA and then decreases, excluding the E9/40% cement compositions. The working time for the E9/40% cement increases by a factor of 3 between 30 and 45 wt % HA, but does not show the same rate of increase between 45 and 60 wt % HA. A similar increase in working time between 30 and 45 wt % HA is observed with the higher PAA concentration cements of the same molar mass,

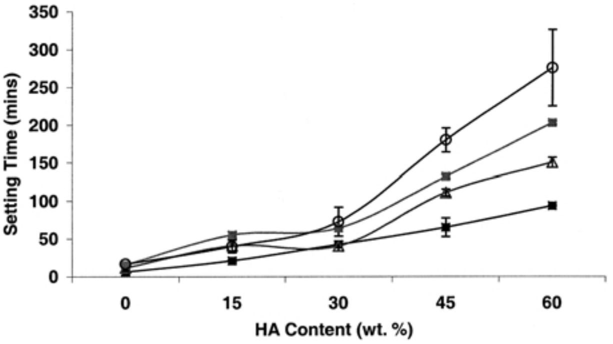

Figure 2 Setting times for the E11/50% (-■-), E9/60 (-△-), 50(-■-) and 40% -○- cements.

increasing approximately by a factor of 2. The working time of the E11/50% cements increases up to 45 wt % HA and then decreases, but does not exhibit a significant increase between 30 and 45 wt % HA. At a low PAA concentration, a given divalent metal ion is more likely to become associated with two carboxylate ions in the same polymer molecule than at a higher concentration. Intramolecular bonding will not lead to gelation and therefore a greater percentage neutralization is necessary at the gel point for more dilute solutions. Hence, the difference in working times with the E9/40% cements. Wall *et al.* [8] reported a similar finding.

The 60 wt % HA cements in this study show a decrease in working time compared to the 45 wt % HA cements. Fig. 2 shows that the setting times continue to increase with all HA contents. A decrease in compressive strength with 60 wt % HA is also observed for the E9/50% and E11/50% cements after one day (Fig. 3). However, after 28 days the E11/50% cement containing 60 wt % HA shows an increase in compressive strength. This behavior, coupled with the fact that the working and setting time of the cements decrease as the ZnO component increases, suggest that it is not only the charge of the cations that affects the association between the inorganic cation and polyacrylate ion, but that the size of the ion also has an influence. This finding was also reported elsewhere [8]. If greater proportions of ZnO result in a faster set, the difference in working and setting behavior observed in Figs 1 and 2 may be due to the difference in size between the Zn^{2+} and Ca^{2+} ions. These cements may set via a two-step setting mechanism, where a zinc polyacrylate species causes primary hardening of the cement and later the formation of calicum polyacrylate leads to a second post-hardening step. A similar mechanism is believed to occur with glass polyalkenoate cements [17].

Fig. 2 shows the setting times for the same cement compositions presented in Fig. 1. It is clear that the setting time increases with HA content, including 60 wt % HA compositions. A significant increase is observed with 45 wt % HA. However, the introduction of 30 wt % HA does not seriously prolong the setting times of these polycarboxylate cements. Also, up to 45 wt % HA can be introduced without decreasing the 24 h compressive strength (Fig. 3). Furthermore, the compressive strengths show a possible plateau between 15 and 45 wt % HA (Fig. 3). Bagnall *et al.* [18] reported similar trends.

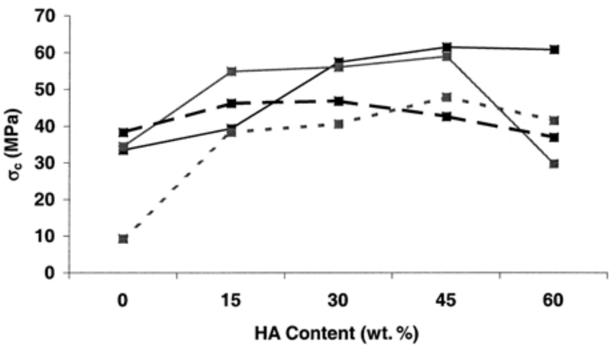

Figure 3 Compressive strengths of the E11/50% cements at 1 day (-■-) & 28 days (—■—) and the E9/50% cements at 1 day (-■-) and 28 days (—■—).

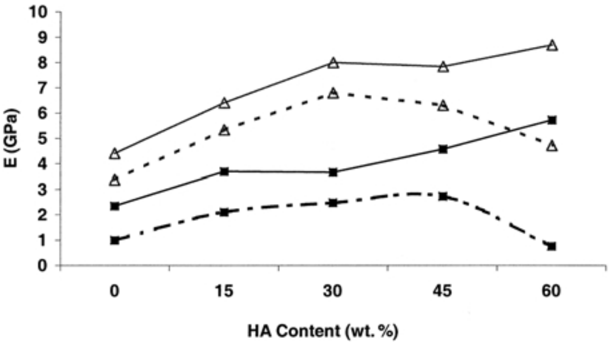

Figure 4 Young's Moduli of the E11/50% cements at 1 day (-■-) and 28 days (—■—) and the E9/60% cements at 1 day (-△-) and 28 days (—△—).

There is also an increase in the compressive strength with time, although the maximum compressive strengths are generally obtained after seven days. This finding suggests that crosslinking continues with time. A similar result was also observed for zinc polyalkenoate cements [19]. On the other hand, the compressive strength of glass polyalkenoate cements increases with time up to 28 days [20–22]. Hydration of the metal–poly(acrylate) complexes [23] was originally believed to be the mechanism behind the increase in strength of glass polyalkenoate cements. However, the identification of a siliceous silica gel [24] has been implicated in a ''secondary'' setting reaction, where the growth of a hydrated silicate phase, and not the formation of metal carboxylates, has been held responsible for the increase in moduli [20, 25, 26] with time [27]. However, this mechanism does not explain the increase in modulus with time, obtained with the cements in this investigation (Fig. 4). Increases in the modulus with HA content are also observed, although it takes 28 days for some of the 60 wt % HA cement compositions to obtain higher moduli than the lower HA content cements. As the cement compositions in this study are based on ZnO/HA compositions and do not contain any silicate forming components, it is safe to say that increased ionic crosslinking is the main reason behind any increases in strength. The mechanical results obtained in this study with respect to HA content, suggest that the modulus of the HA component does contribute to the final properties. However, the observed increases in mechanical properties with time indicate that some sort of interaction occurs between the HA and PAA components.

HA has been chosen to improve the composite nature of polyalkenoate based cements as polycarboxylates are known to adhere to HA [18]. PAA is also employed as an organic additive [28] because of its ability to strongly bind calcium ions. This was the motive behind the selection of PAA is studies involving the polyester-ether composite Polyactive™ [29–31]. However, there is much dispute in the literature about the exact nature of interaction between HA and the matrix which surrounds it. HA was reported to act as an unreactive filler in polyethylene composites [32] due to the fact that the moduli monotonically increased with HA additions of up to 45 wt % HA. Nicholson [33] attributed the slower setting reaction and weaker cement properties to the incorporated HA in glass polyalkenoate cements. Strong ZnO–PAA interactions were observed after four days for

HA–ZnO–PAA cements where the HA was reported to act as an inert filler [34]. However, none of these studies investigated the influence of aging time with regard to the HA component.

4. Conclusions

These studies indicate that, although the addition of HA increases the working and setting times of these polyalkenoate based cements, at least 30–45 wt % HA can be incorporated into the cements without significantly affecting performance. Compressive strength reaches a maximum after seven days, whilst crosslinking continues to increase the moduli after 28 days aging. This observation may provide evidence against the argument that a silicate phase, in glass polyalkenoate cements, participates in changes to the mechanical properties. Since the hardening reaction in these cements basically consists of a crosslinking process of the polyacrylate chains, understanding the formation of the microstructure is extremely important if the mechanical properties of such cements are to be improved. The chemistry of these cement systems will therefore be subject to future investigations.

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