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Injectable acrylic bone cements for vertebroplasty based on a radiopaque hydroxyapatite. Formulation and rheological behaviour

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Abstract The utilization of injectable acrylic bone cement is crucial to the outcome of vertebroplasty and kyphoplasty. However, only a few cements that are in clinical use today are formulated specifically for use in these procedures and even these formulations are not regarded as "ideal" injectable bone cements. The aim of this work is to prepare bioactive bone cements by adding strontium hydroxyapatite (SrHA) to a cement formulation based on polymethylmethacrylate. Thus, the cement combines the immediate mechanical support given by the setting of the acrylic matrix with optimum radiopacity and bioactivity due to the incorporation of the SrHA. Formulations of bioactive cement were prepared with 10 and 20 wt% of SrHA as synthesised and after a surface treatment with the monomer. Cements loaded with treated particles showed an enhancement of their handling properties, and hence, an improvement on their rheological behaviour, injectabilities and compressive parameters. Further experiments were also carried out to determine their bioactivity and biocompatibility and results appear in other publication.

1 Introduction

Vertebroplasty (VP) and Kyphoplasty (KP) are minimally invasive surgical procedures that have recently been introduced for the treatment of vertebral diseases [1]. In VP, bone cement is injected into the damaged vertebra to strengthen it thus preventing further microfractures and associated pain. The aim of KP is pain relief combined with restoration of vertebral body height and reduction in kyphosis. This is achieved by 'expanding' the fractured vertebra with a balloon to create a cavity, which is then filled with cement. Both procedures have a very low complication rate if properly performed by well trained clinicians using appropriate cement, skill and high-quality imaging [2]. VP was first performed for the treatment of vertebral hemangiomas [3], but the success of this procedure has broadened the indications as well to include spinal metastasis and osteoporotic fractures [4].

The injectable bone cement is crucial to the outcome of VP and KP. Its desirable properties include easy injectability, high radiopacity and mechanical efficiency. Only a few cements that are in clinical use today are formulated specifically for use in these procedures and even these formulations are not regarded as "ideal" injectable bone cements [5]. Acrylic bone cements based on polymethylmethacrylate (PMMA) along with calcium phosphate cements are the main types of formulations available in the market for application in these techniques. Commercial formulations of both families suffer from some drawbacks. The most relevant for the acrylics are the exothermic reaction and poor adhesion to bone surfaces and for the inorganics, the rapid resorption and poor mechanical properties. When developing a bioactive material, both mechanical and biological characteristics must be considered and a balance achieved [6]. Hence, injectable bioactive bone cements are being demanded to be used in this application, the development of composite formulations being the one of choice. Certain compositions of glasses, glass ceramics containing apatite and wollastonite, and calcium phosphate ceramics such as hydroxyapatite

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(HA) or tricalcium phosphate, have been reported to form a strong chemical bond with bone [7]. Taking advantage of this, experimental bioactive bone cements have been developed by mixing a bioactive powder with the resin and PMMA bone cements have been formulated by incorporation of some of these compounds to enhance its bond with bone [8–10]. Parallel bioactive acrylic bone cements have been developed based on the Bowen molecule 2,2-bis[*p*-(2′-hydroxy-3′-methacryloxypropoxy) phenyl] propane (bis-GMA). Some bioactive cements have been reported with incorporation of bioactive glass and tri-calcium phosphate [11] or HA granules [12]. Based on this rationale, commercially available formulations specially designed for VP based on composites are in the market. An example is the bone cement Orthocomp,™ an injectable, non-resorbable, bone-bonding cement which is undergoing a phase of clinical trials in France for use in vertebroplasty. This cement is composed of bis-GMA and bisphenol A ethoxylated dimethacrylate (Bis-EMA) as the resin, and reinforced with bioactive fillers [13]. Vertebral bodies (VB) augmented with this cement present lower heating injury [14], and recovered their initial stiffness with lesser volumes of cement compared with PMMA [15].

Another composite formulation has been developed as a synthetic cortical bone filler, Cortoss™. The cement is formulated with approximately 31 wt% high molecular weight monomers (bis-GMA and bis-EMA diluted with triethylene glycol dimethacrylate (TEGDMA) with dihydroxyethyl-*p*-toluidine (DHEPT) as activator, and reinforcing components such as glass-ceramic particles, barium boro-alumino-silicate glass and amorphous silica, with benzoyl peroxide as initiator of the radical polymerisation. The glass ceramic fillers (5–50 μm) are surface treated with (3-trimethoxysilyl) propyl methacrylate (γ-MPS) to couple the filler particles with the polymer matrix. This product has received marketing approval in Europe and Australia, and in the U.S.A., clinical trials have been initiated to evaluate Cortoss™ in the treatment of vertebral compression fractures and to augment screws that fail to hold in osteoporotic bone. This highly crosslinked formulation presents some advantages compared to those of plain PMMA, mainly the formation of bone growth directly on its surface [16].

Recently, Li et al. [17] have developed a novel injectable bioactive bone cement composed of strontium-containing hydroxyapatite (SrHA) and Bis-GMA specifically for use in spinal surgery. SrHA has stronger mechanical properties, better bioactivity than pure HA, and similar biocompatibility. Moreover, its radiopacity allows it to be radiographically visualised without the need for additional radio contrast material. The bioactivity of these cements has been proved in vivo giving suitable osteointegration [18].

In this paper, we report the preparation of a bioactive bone cement by adding SrHA to a cement formulation based on PMMA. Thus, the cement combines the immediate support given by the setting of the acrylic matrix with optimum in vivo longevity due to the incorporation of the SrHA, which should elicit an osteogenic response and the osteointegration of the implant. The characteristics of the curing and main physical properties were evaluated for application of such formulations in minimally invasive surgery.

2 Materials and methods

2.1 Materials

Methyl methacrylate (MMA) (Merck), *N*, *N*′, dimethyl-4-toluidine (DMT) (Merck) and barium sulphate for radiological examination ($BaSO_4$) (Merck) were used as received without further purification.

As in other works [19], we used a mixture of two kinds of PMMA beads of different sizes: 80% (w/w) of Colacryl (Bonar) with a diameter of 118.4 μm and a size distribution which goes from 60 to 200 μm and 20 wt% of Plexigum (Rohm and Haas) with a diameter of 69.7 μm and a distribution which goes from 20 to 150 μm. Benzoyl peroxide (BPO) (Merck) was used as the polymerization initiator.

P_2O_5 (Scharlau), $NaHCO_3$ (Scharlau), $Ca(OH)_2$ (Riedel-de-Häen) and $Sr(OH)_2$ (Riedel-de-Häen) of reagent grade were used to synthesise the HA.

2.2 Methods

2.2.1 Synthesis and characterisation of the bioactive filler

SrHA powder was synthesised as described by Li et al. [17]. To this end, a solution of 0.2 mol of P_2O_5 and 0.2 mol of $NaHCO_3$ in 100 ml of water was added dropwise over a solution of 0.5 mol of $Ca(OH)_2$ and 0.1 mol of $Sr(OH)_2$ in 150 ml of water maintained under stirring. Once a pH of 9.5 was obtained by adding HCl, the mixture was allowed to react at room temperature for 3 days. Then, the reaction medium was neutralised and the solid obtained was filtered. After drying at 500°C for 24 h, the powder was milled in a mortar. The characterisation of the solid was carried out by means of IR spectroscopy and X-ray diffractometry.

Additionally, in order to enhance the compatibility of the filler with the matrix, and improve the mixing capacity and injectability of the new cements, a part of the obtained powder was treated with the MMA monomer as described by Zhao et al. [20]. The treatment consisted mainly of mixing the dry powder with the MMA and ultrasonicating the mixture for 24 h. After centrifugation, the powder was dried at 60°C to eliminate the unadsorbed monomer. The

MMA adsorbed content in the filler after this treatment was estimated to be 0.36 wt% by thermogravimetric analyses.

2.2.2 Preparation of bone cements

The preparation of the acrylic bone cements was carried out following the method used for classical bone cement described in the ISO 5833 Standard [21]. The bone cement components were hand-mixed. The bioactive bone cements were formulated using a solid: liquid ratio of 2:1. The liquid component consisted of MMA monomer and DMT as the activator for the polymerisation reaction (1 vol% with respect to the liquid phase), in all cases. The solid component consisted of PMMA beads (Colacryl/Plexigum 80/20), the corresponding bioactive powder, and BPO (1.25 wt% with respect to the solid phase). SrHA was added in two different ways: treated with MMA (SrHA-t samples) and untreated (SrHA samples). Formulations of bioactive cements were prepared with 10 and 20 wt% of SrHA in the solid phase. Despite having a higher percentage of bioactive filler is desirable from the bioactivity point of view, the addition of higher quantities of SrHA did cause a deterioration of the handling properties.

As controls, two other formulations were prepared, a radiolucent one and another with 10 wt% of $BaSO_4$ in the solid phase.

2.2.3 Characterisation of bone cements

Although no specific standard exists for cements for use in VP and KP, in order to use some reference, the characterisation of the cements was carried out following the methods used for acrylic bone cements for arthroplasty described in the ISO 5833 Standard [21]. The exothermic reaction produced by the mixing of powder and liquid components was monitored according to this standard. The maximum temperature attained by the bulk was recorded and the setting time was calculated as the time in which the bulk temperature was midway between the maximum and room temperature.

The residual monomer content was measured by proton nuclear magnetic resonance (^{1}H-NMR) as described before [22] in a FT-NMR Bruker spectrophotometer operating at 300 MHz. Samples obtained from cements cured at body temperature for 1 h were immediately dissolved in deuterated chloroform with tetramethylsilane as internal standard to obtain the spectra.

The observation of the microstructures of the different formulations was studied by using a scanning electron microscope (SEM Hitachi-S-2700) with an acceleration voltage of 15 kV. The samples were cryogenically broken and the surface fractures were previously gilded.

Weight loss was determined gravimetrically after the immersion of cement sheets ($10 \times 25 \times 1$ mm^3) in simulated body fluid (SBF), which was prepared according to the protocol reported by Kokubo and coworkers [23]. Calculation of elution capacity was performed as described in a previous paper [24], applying the following equation:

$$\%E = \frac{M_0 - M_f}{M_0} \cdot 100 \quad (1)$$

where M_0 is the dry sample weight and M_f, the dry weight after testing.

Evolution of complex viscosity (η^*), storage and loss moduli (G' and G'') and loss tangent (tan δ) as a function of time were measured using a Rheometric Ares rheometer in dynamic oscillation mode at a frequency of 1 Hz using plate–plate configuration. The radius of the plates was 25 mm and the gap between them was 2 mm. The rheometer was used in a constant strain mode with strain amplitude of 1 wt% and measurements were conducted at room temperature (25°C). The procedure was as follows: a chronometer was started up at the moment of mixing both components of the cement. When the dough reaches an homogeneus state, which is noticed by a complete wetting of the powder and a liquid-like consistency of the mixture, it was placed on the lower plate and the measurements were started until the viscosity of the cement was so high that the sample upset the even movement of the plates.

To measure the injectability of the various formulations, we followed the same procedure as described before [24]. Injectability was defined as the weight percent of cement injected into the recipient, expressed as a percentage of the total amount of cement charged into the syringe and injected after the adequate mixing of its components. Mixing time applied to all formulations was 3 min. Injection time was defined as the time between the end of the mixing and the end of the injection, including the purge of the needle. These measurements were run in duplicate.

In order to characterise the mechanical behaviour of the formulations, compressive tests were carried out on specimens stored in air at room temperature and on specimens stored in SBF for 1 month at body temperature. At least six specimens (cylinders with 12 mm of height and 6 mm of diameter) were tested on an Instron 4301 testing machine at room temperature, with a crosshead displacement of 22 mm/min. Yield compressive strength and compressive modulus were determined according to ISO 5833.

An X-ray photograph of the cements was taken using standard clinical General Electric X-ray equipment (set at 25 kV and 4 MAS).

2.2.4 Statistical analysis

For the setting parameters and the characterisation of mechanical properties, mean and standard deviation values were calculated using the 1-way ANOVA statistical

technique. The error protection method used in this research was the Fisher PLSD method and the confidence limit used was 95%.

3 Results

First, the characterisation of the synthesised SrHA was carried out by means of FTIR spectroscopy (Fig. 1a). The spectrum shows in first place the asymmetric peaks of phosphates: flexion vibration of the O–P–O (λ_4) at 564 cm^{-1} and 604 cm^{-1} and tension vibration (λ_3, λ_1) at 1,097 cm^{-1}, 1,030 cm^{-1} and 959 cm^{-1} and, in second place the bands (λ_2) corresponding to carbonate groups at 874 cm^{-1} and (λ_3) at 1,418 cm^{-1} and 1,458 cm^{-1}. Additionaly, the X-ray spectrum (Fig. 1b) is almost identical to that obtained by Li et al. [17] and showed the characteristic bands of HA at the diffraction angles (2θ) of 26.0 and 31.9. In order to characterise the powders, the particle size distributions were measured (Fig. 2). The mean diameter of the SrHA powder was 4.02 μm, whereas the mean diameter of the MMA-treated powder was 6.96 μm, because after the treatment, the size of agglomerates increases slightly. Nevertheless, the distributions of both SrHA were very similar.

Figure 3 shows the time–temperature plots for all formulations. If we compare the new formulations with the control ones, we can affirm that the addition of SrHA, untreated or treated, did not significantly affect the maximum temperature. Alternatively, the addition of both forms of SrHA increased the setting times. This increase was significant in formulations containing 20 wt% SrHA or more since the high percentage of filler impedes the mixing of the cement and delays the polymerization process. Surface treatment of the particles reduced the amount of MMA required to achieve sufficient wetting of filler particles, so the mixing step was faster and thus, the setting time was significantly reduced with respect to the cement with untreated filler.

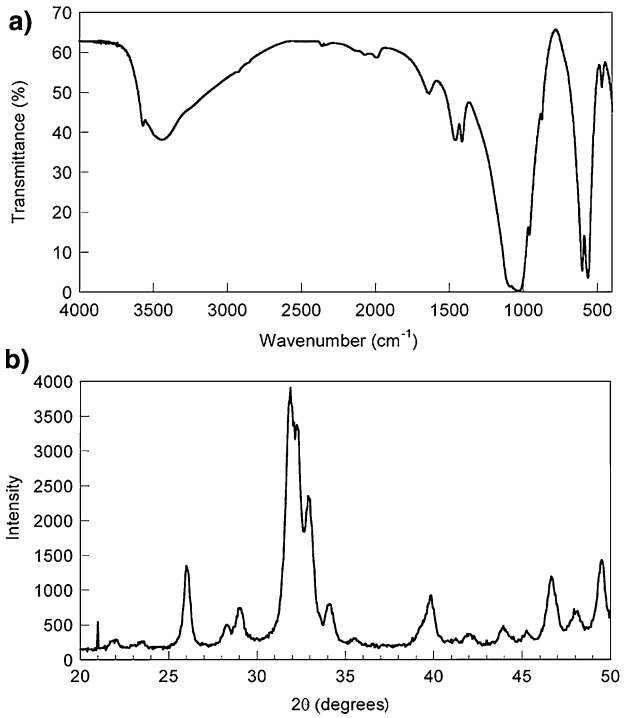

Fig. 1 The chemical composition of the synthesised powder analysed by FTIR (**a**) and X-ray diffractometry (**b**)

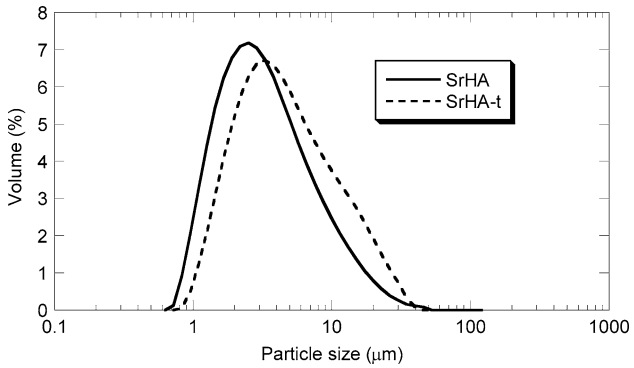

Fig. 2 Particle size distributions of the synthesised and treated powders

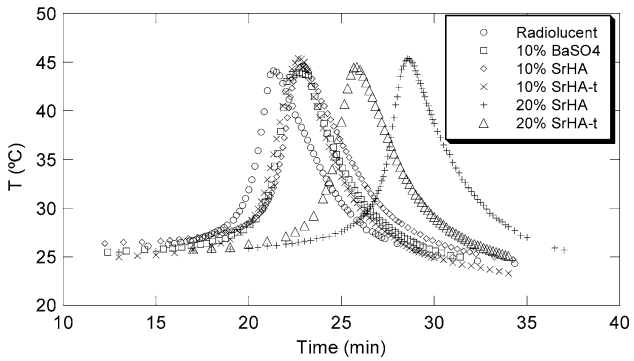

Fig. 3 Kinetics of the setting at 23°C of all the cements studied

Determinations of residual monomer content (Table 1) showed no statistical differences between the new formulations and the control ones. It is important to note that the surface treatment with MMA of the SrHA particles did not result in a significant increase of this parameter.

Representative samples of the cryogenically broken specimens of the cements with treated and untreated SrHA were studied by SEM and are shown in Fig. 4. Although in all the cements the dispersion of the SrHA particles should be enhanced, the compatibility of the particles is higher when monomer treatment is applied (Fig. 4a, c). The difficulties encountered during mixing of the untreated cements gave rise to a higher porosity. In the 20 wt% SrHA cements (Fig. 4d), we can clearly observe an insufficient

Table 1 Residual monomer content after 1 h of curing at 37°C (% M_r), results of the elution tests (%E) after 1 month of immersion in SBF at 37°C and injection properties (time of injection, t_{inj}, and injectabilty, I) of all the cements studied

Cement	M_r (%mol)	E (%)	Injection properties	
			t_{inj} (min)	I (%)
Radiolucent	2.25[a] (0.24)[b]	0.21 (0.02)	5.43 (0.28)	83.17 (1.11)
10% $BaSO_4$	2.38 (0.24)	0.32 (0.01)	5.91 (0.31)	78.20 (1.42)
10% SrHA	2.22 (0.29)	0.84* (0.06)	6.07 (1.80)	79.71 (1.70)
10% SrHA-t	2.56 (0.25)	0.29[t] (0.03)	6.89* (0.44)	83.25*,[t] (1.44)
20% SrHA	2.42 (0.13)	1.48* (0.01)	6.90* (0.42)	78.22 (2.39)
20% SrHA-t	2.34 (0.16)	0.96*,[t] (0.06)	7.50* (1.44)	83.12*,[t] (0.36)

[a] Values with statistical differences with respect to 10% $BaSO_4$-containing cement (*) and with respect to the same formulation with untreated SrHA([t]) are indicated

[b] Values in parentheses indicate the standard deviation

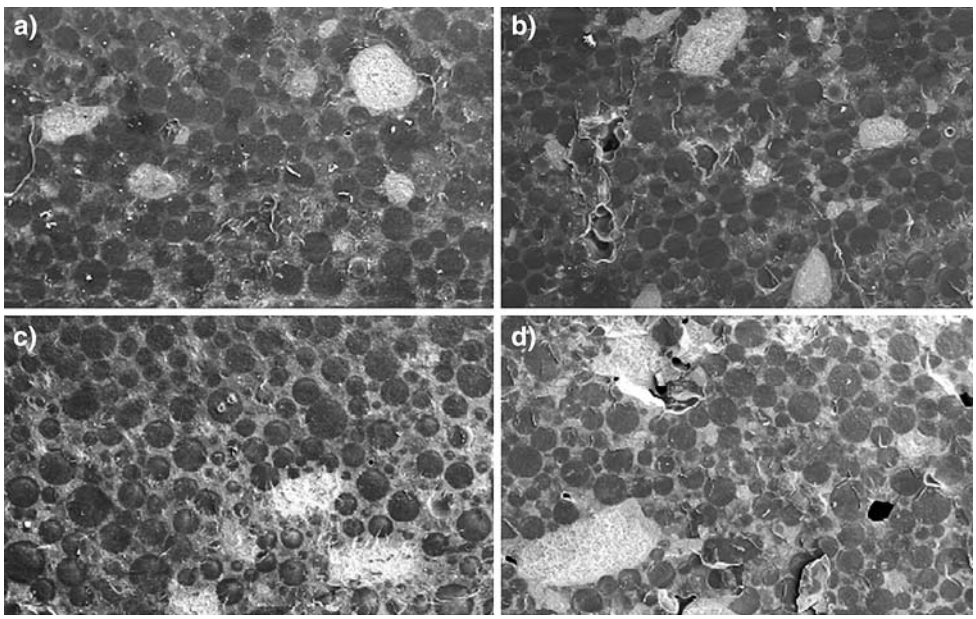

Fig. 4 SEM micrograph of broken surfaces of SrHA-containing cements. (**a**) 10 wt% SrHA-t, (**b**) 10 wt% SrHA, (**c**) 20 wt% SrHA-t and (**d**) 20 wt% SrHA

interaction between the matrix and the filler. The lower compatibility and the higher porosity gave rise to weak points in which fracture was produced by this lack of adhesion.

Table 1 also shows the results of the elution test after 1 month of immersion in SBF at 37°C. Incorporation of SrHA particles to the cement formulations significantly increased the values of weight loss in line with the filler content with respect to cement containing the $BaSO_4$, due to the higher polarity and solubility of this filler. However, in the case of cements with treated filler, this parameter hardly increased at all. In the case of the 10SrHA-t cement no statistical differences with respect to the radiopaque control were observed. This behaviour can be attributed to the MMA treatment that hydrophobises to some extent the surface of the SrHA particles. Furthermore, the higher porosity of the cements formulated with non-treated particles contributes to a higher water absorption and hence a higher elution.

Oscillatory measurements allowed us to characterise the rheological behaviour of the new formulations during the curing, which is of capital importance for VP cements intended for syringe usage. From the moment of mixing, the cement goes through a viscoelastic phase, where it changes from having predominantly liquid-like properties (just after the mixing of the two phases) to having predominantly solid-like properties once set [25]. The evolution of complex viscosity (η^*) (Fig. 5a) it's similar for all formulations since, as we demonstrated in a previous paper [24], the PMMA beads employed in the solid phases are the same. The differences found in the evolution of η^* are due to the differences found in the polymerisation kinetics. In the case of the 20 wt% SrHA-cement, the poor handling properties and its slow polymerisation made the

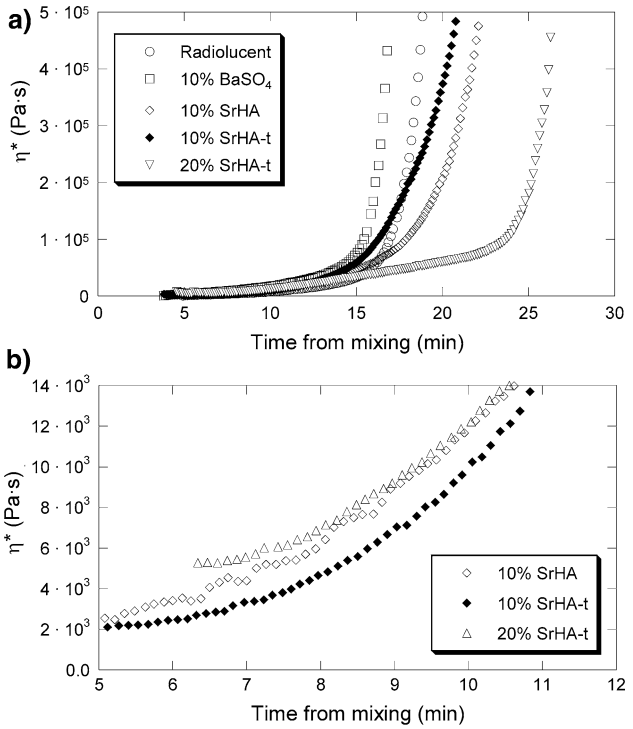

Fig. 5 Evolution of complex viscosity with the time elapsed from mixing for all formulations (**a**) and magnification of the beginning moments for cements filled with the HaSr filler (**b**)

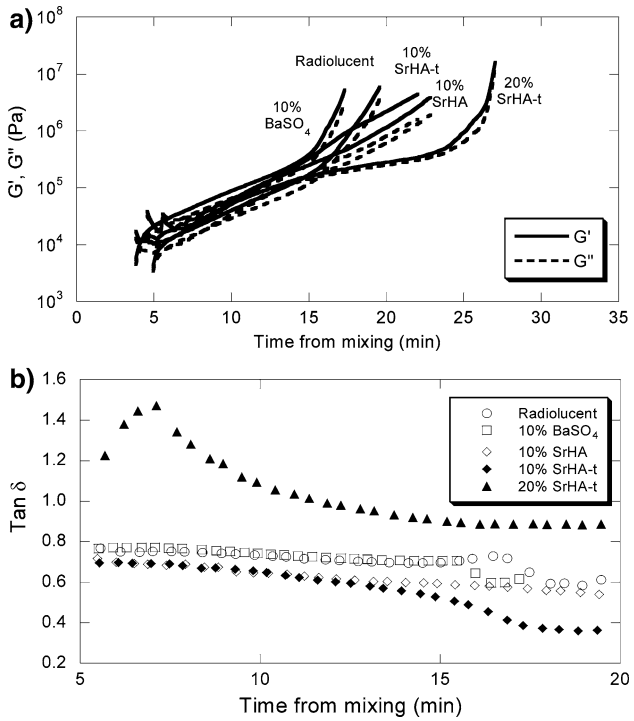

Fig. 6 Evolution of storage and loss moduli (**a**) and loss factor (**b**) as a function of the time elapsed from mixing for all formulations

evolution of η^* unappreciable during the experiment compared with the other formulations. If we look at the magnification (Fig. 5b), we can appreciate that the treatment of SrHA particles decreased the η^* just after mixing. The 20 wt% SrHA-t cement showed initial values of η^* similar to the 10 wt% SrHA cement, although it had the double quantity of filler. Moreover, an increase on the homogeneity of the cement mass can be noticed from the reduction of the irregularities found in the evolution of η^* of the SrHA-t loaded cements.

From the rheological measurements, viscoelastic parameters are also obtained. The storage or elastic modulus (G') reflects the recoverable portion of the energy imparted by the applied strain. The loss modulus (G'') is a measurement of the viscous behaviour of the material that leads to the dissipation of part of the energy imparted by the applied strain. The loss tangent (tan δ) is defined as the ratio G''/G'. Representative plots of these parameters versus time from mixing are given in Fig. 6. This last parameter will move from ∞ to 0 if we pass from a Newtonian liquid to an ideal elastic material [19]. The very beginning of the moduli plots in Fig. 6a indicates the moment when a solid-like behaviour becomes more noticeable than that of the liquid-like. After that, all the dough cements show an increase of both moduli as the setting proceeds, as in the case of complex viscosity, with a final increase attributable to the increasing polymerization rate. Since the polymerization of 20 wt% SrHA-t cement is slow, we can clearly appreciate the complete evolution of the moduli on the setting, whereas for the 20 wt% SrHA formulation, the evolution is negligible. We observe that in all cases elastic and storage moduli follow very similar plots. However, in the case of the reference formulations we can appreciate that the rate of increase of storage and loss moduli becomes faster at earlier moments than those of SrHA-containing formulations.

Tan δ (Fig. 6b) shows a slow and progressive change as a function of time. As we have explained in previous papers, this change is closely related to the performance of injectability [19]. We can say that a practically constant value of tan δ or a slight increase of it will be of benefit to the injectability of these formulations.

Injectability results are summarised in Table 1. Time of mixing employed was 3 min for all formulations. Injectability percentages are high for all formulations due to the PMMA beads employed in the solid phase [9]. Moreover, there is a slight increase on I (%) for the SrHA-t cements, but the most important feature of these cements with treated filler is their enhanced handling properties. The strength needed to inject these cements is lower than for the cements with untreated filler. The untreated cements, although fluid, tend to compress at the bottom of the syringe which makes it necessary to apply great force to inject them. Alternatively, cements with treated particles flow more easily, it seems that the treatment of particles has a

lubricant effect, allowing problem-free injection. In Fig. 6b, we can observe that both treated cements have a negative slope at high times, showing that the viscous component of the mixture becomes higher than the elastic one. Since this behaviour appears at longer times than injection time it doesn't affect to the greater injectability of these cements.

Compression test results are presented in Table 2. For these formulations, the addition of a radiopaque agent decreases the compression resistance with respect to the radiolucent formulation, but the difference is only significant for cements loaded with untreated SrHA particles. Compared with the $BaSO_4$-containing cement, the experimental formulations did not show statistical differences. The surface treatment improved the resistance of the cements due to a better integration of the filler particles with the matrix, but this improvement is significant only in the case of the cements with 20 wt% of filler content. Regarding modulus, cements with SrHA present higher values than control formulations, and this parameter increased with the filler content and the surface treatment (significant for 20 wt% loaded formulations). After 1 month of immersion in SBF at 37°C, the plasticizing effect of the absorbed water decreased significantly both strength and modulus. Experimental formulations showed no statistical differences with respect to the $BaSO_4$ containing cement, except for the 20 wt% SrHA-treated cement, which exhibited a significant increase in compression strength. Moreover, although compression modulus has a similar behaviour compared to dry specimens, the plasticizing effect is clearly more noticeable in the SrHA-containing cement.

The radiopacity of cement formulations is shown in Fig. 7. As we can clearly observe, cements with 10 wt% of radiopaque agent showed similar radiopacity to the $BaSO_4$ containing cement. The X-ray visibility obviously improved as the filler content increased. Moreover, we can appreciate the improved homogeneity of the samples with treated SrHA particles in the photograph, which in turn enhanced the visibility of the 20 wt% SrHA-t cement.

Table 2 Results of the compression tests performed in dry specimens and in specimens stored in SBF for 1 month at 37°C

Composition	Dry		Wet	
	σ_c (MPa)	E_c (MPa)	σ_c (MPa)	E_c (MPa)
Radiolucent	112[a] (4)[b]	1800 (100)	103 (4)	1620 (60)
10% $BaSO_4$	107 (5)	1700 (40)	93 (5)	1520 (50)
10% SrHA	104 (4)	1900* (70)	94 (2)	1690* (60)
10% SrHA-t	109[t] (1)	1920* (30)	96 (2)	1720* (50)
20% SrHA	106 (4)	1980* (80)	90 (6)	1720* (90)
20% SrHA-t	111 (2)	2070*,[t] (40)	98*,[t] (1)	1780* (50)

[a] Values with statistical differences with respect to 10% $BaSO_4$-containing cement (*) and with respect to the same formulation with untreated SrHA([t]) are indicated

[b] Values in parentheses indicate SD values

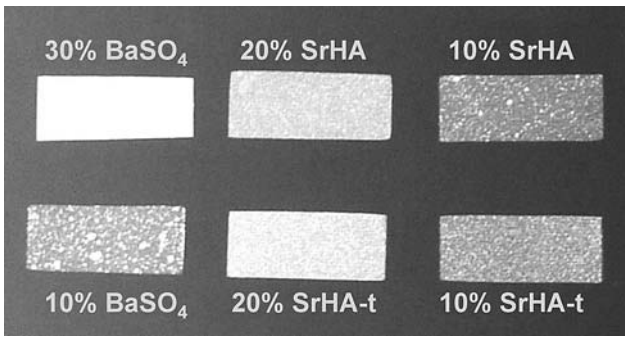

Fig. 7 X-ray photograph of the cements

4 Discussion

The success of VP and KP has broadened their indications, remaining the scope of both techniques the same: immediate mechanical stabilization of the vertebral body in order to obtain rapid pain relief. This is successfully accomplished using acrylic bone cements. However, they fail in long-term fixation with the surrounding tissues, which compromise the lifelong stabilization of the vertebrae. Thus, the research on new formulations with ingredients, which allow bioactivity, should provide an optimum in vivo longevity.

However, before testing the possibilities of bioactivity some other properties must be evaluated. First of all, we observed that the incorporation of SrHA up to 20 wt% caused a worsening of the handling and mixing properties, so a surface treatment of the particles to improve the compatibility of the SrHA with the liquid monomer was mandatory. Taking into account the good results obtained by Zhao et al. [20], a treatment with MMA was chosen. The procedure was simple and did not introduce additional ingredients to the formulation, which could create problems of toxicity. The surface treatment of the particles resulted in an immediate improvement of the mixing behaviour, which significantly reduced the long setting time of the cements with 20 wt% of filler. This modification did not result in a significant increase of the residual MMA content after 1 h of reaction at 37°C and it allowed the enhancement of the interface between the monomeric matrix and the radiopaque filler.

As the rheological properties concerns, the improvement of the cement mass homogeneity resulted in a decrease of η^*, just after mixing. Later, when the polymerization is the process which controls the increase of η^*, the cements

filled with SrHA-treated particles showed a faster increase of η^*. This behaviour is very interesting, since the cement could provide immediately the necessary stabilization to the lesion once the injection is performed. Moreover, in the injection tests, cements with treated particles flow more easily. It seems that the treatment of particles has a lubricant effect, allowing problem-free injection.

The surface treatment improved the compression resistance of the cements due to a better integration between the filler particles and the matrix, although this improvement is notable only in the case of the cements with higher contents of SrHA, where the problems in the mixing were significant. The plasticizing effect of the water absorbed is partially hidden by the reinforcing effect of the bioactive charge. The improved homogeneity and the radiopacity of the samples with treated SrHA particles could be appreciated in the X-ray image.

Nevertheless, the surface treatment could hydrophobize the surface of the SrHA particles, limiting their release. This release is believed to have a positive effect on the bioactivity as it is expected to stimulate bone formation. Moreover, the voids left by the dissolved particles could allow bone ingrowth. Further work is being performed to determine the effect on this behaviour on the bioactivity of the cements [26].

In conclusion, while it is clear from this research that cements formulated with treated SrHA offer enhanced handling properties, optimum injectability and are capable of withstanding wear conditions, additional experiments are needed to determine their bioactivity and biocompatibility and appear in a second publication [26]. However, we can advance that in vitro bioactivity and in vivo biocompatibility were evaluated after immersion of the cement samples in a physiological-like fluid and through human fibroblasts culture, respectively. Both, the deposition apatite layer and the cell and materials interaction data show very interesting results.

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