Acrylic Bone Cements Modified With Bioactive Filler

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Summary: Bioactive cuttlebone *Sepia officinalis* particles that contain collagen were used to fill poly (methyl methacrylate-*co*-styrene) bone cements, varying size and concentration of filler particles. Cuttlebone was characterized by X-ray diffraction and plasma atomic emission spectrophotometer. Maximum reaction temperature and cement setting time were determined for composites and reference (copolymer without filler), along with NMR determination of residual monomer concentration. Mechanical properties characterization included stress-strain, bending, compression, fracture toughness and storage modulus tests. Mechanical results for composites filled with 10 and 30% weight of cuttlebone, complied with norm requirements which opens the possibility for using cuttlebone particles as bioactive filler.

Keywords: acrylic; bone cement; bioactive filler; cuttlebone; collagen

Introduction

Acrylic bone cements are widely used in orthopedic surgery to fix artificial prostheses where the cement grout serves to immobilize the implant and to transfer loadings to the bone.[1] Prostheses have an average lifetime of 12 to 15 years,[2,3] which for young patients, is a short lifetime. A reduction on average lifetime of the prostheses has been associated with temperature increase due to the polymerization reaction (which may cause thermal necrosis to adjacent tissues).[4] In addition cemented prostheses fail due to septic processes, breakage of the acrylic cement or prosthesis, or to the loosening of bone/cement and cement/prosthesis interface.[3] For such reasons, several paths have been investigated to increase lifetime of prostheses.[1] One path is the incorporation of bioactive particles to promote bone growth around an implant.[1] Because almost 98 wt% of the total calcium in human organisms is present in the osseous structure as hydroxyapatite crystals $C_{10}(PO_4)_6(OH)_2$, calcium phosphate $Ca_3(PO_4)_2$, and calcium carbonate $CaCO_3$,[5] in an attempt to increase biocompatibility and to promote bone growth around an implant, several studies incorporating hydroxyapatite (HA) and calcium phosphate have been reported.[1,6–8] The presence of bioactive particles, besides modifying mechanical properties of the bone cement,[8,9] also affects curing characteristics. Morejón et al., reported that when using HA as filler in a poly (methyl methacrylate-*co*-styrene) bone cement, lower curing temperature peaks than for the unfilled cement were obtained.[7]

In the search of fillers with high potential for osteointegration in human applications, it has been reported that the use of cuttlebone particles from *Sepia officinalis* as a bioactive filler on acrylic cements leads to osteointegration due to its collagen and calcium carbonate content.[10] As a consequence, it is important to determine the influence of size and concentration of cuttlebone particles to be used in acrylic bone cements, to comply with norm

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requirements of mechanical properties. For that reason, the effect of cuttlebone particle size and concentration on mechanical properties and curing kinetics of an acrylic bone cement filled with *Sepia officinalis* cuttlebone is reported here.

Experimental Part

Beads of poly (methyl methacrylate-*co*-styrene) were prepared by suspension polymerization. Methyl methacrylate, styrene (monomers) and benzoyl peroxide (initiator) were acquired from Aldrich Chemical Co. Poly(vinyl pyrrolidone) PVP-K90 (Spectrum Chemical) was used as stabilizer of the suspension polymerization system. The polymerization was carried out at 80 °C using a comonomer ratio of 80/20 wt/wt (methyl methacrylate/styrene). The polymer average molecular weights were: $\overline{M}_n = 130{,}000$ and $\overline{M}_w = 196{,}000$ (measured by GPC). The beads have spherical shape with average diameter of $32.1 \pm 8.9\,\mu m$.

Cuttlebone of the *Sepia officinalis* was grinded using a hammer mill (Mikro Pulverizer type SH. Particles were separated by sieve screening in three ranges: 74–53 μm, 53–37 μm and less than 37 μm, (270, 400 and > 400 mesh respectively).

Cuttlebone powders were examined with an X-ray Siemens Difractometer (D500) to identify crystal structures. Cuttlebone chemical composition was determined using an inductively coupled plasma atomic emission spectrophotometer, spectroflame FM-03, (ICI/AES). To determine collagen content the cuttlebone was digested using an aqueous solution of 0.1 N hydrochloric acid (Productos Químicos Monterrey).

For cement preparation a 2/1 powder/liquid ratio was used in all formulations. The powder component consisted of 2.0 wt % recrystallized benzoyl peroxide, 10.0 wt % barium sulfate (Aldrich Chemical Co.) as radiopacifier, cuttlebone particles in different amounts (0, 10, 30 or 50 wt %), and poly (methyl methacrylate-*co*-styrene) beads to complete 100 wt %.

Chemical composition of the liquid part was 97.3 wt % methyl methacrylate, 2.7 wt % N,N dimethyl-p-toluidine (accelerator), and 80.0 ppm of hydroquinone (99% pure), all from Aldrich Chemical Co.

Setting time and maximum temperature were determined following ASTM F451 procedure. Temperature was followed using a thermocouple type k connected to a multimeter (Omega HH23. The average of three measurements is reported. Residual monomer content was determined by ^{1}H-NMR using a Varian Gemini 200 (Palo Alto, CA).

For tensile tests, specimens were prepared mixing a cement formulation at room temperature and then inserting it into a mould just before dough time. The filled mould was pressurized at 25 °C using a hydraulic press and held there until the cement hardened (approximately 20 min). Test specimens complied with ASTM D-638[11] for type V specimens. Tensile tests were carried out using a United 5802 Universal Testing Machine (Huntington Beach, CA, USA) at 1 mm/min crosshead speed. Average values of 5 tests are reported.

Compression test specimens were made following ISO 5833[12] procedure. Cylindrical samples having 6 ± 0.1 mm diameter and 12 ± 0.1 mm height were used. Average values of 5 tests are reported.

For bending tests, rectangular specimens of $63.5 \times 12 \times 3.3\,mm^3$ were prepared following ASTM D-638[11] procedure. Tests were made using a United 5802 Universal Testing Machine (Huntington Beach, CA, USA). Each value is the average of 5 tests.

Fracture toughness (K_{IC}) was measured using compact tension (CT) test specimens following ASTM D5045.[13] Tests were carried out at a crosshead speed of 1 mm/min, using a United 5802 Universal Testing Machine (Huntington Beach, CA, USA). Each value is the average of 5 tests.

Mechanodynamic tests were carried out in a Rheometrics rheometer RDS II, using the torsion bar fixture, in samples of $40 \times 12 \times 3.3\,mm^3$, with 0.1% deformation and frequency of 1 Hz. Each value is the average of 2 tests.

Results and Discussion

Since the clinical study of cements filled with bioactive cuttlebone particles from *Sepia officinalis* demonstrated its usefulness for osteointegration,[10] this study serves as a complement, justifying the use of such composite by fulfilling curing kinetics and mechanical requirements.

By X-ray diffraction it was determined that cuttlebone is composed mainly of aragonite, ($CaCO_3$), small amounts of calcite, ($CaCO_3$), and hydroxyapatite $Ca_5(PO_4)_3(OH)$.

By chemical analysis it was found that cuttlebone particles have 48 wt % of Ca, 2.09 wt % of P and 0.57 wt % of Na. From these data, it was determined that the cuttlebone has 89.9 wt % of calcium carbonate; the rest is water, collagen and calcium phosphate.

For the following discussion, identification codes for composites composition are shown in Table 1.

Figure 1, shows the evolution of temperature with reaction time for composites prepared using different particle size and particle concentration. In all cases, there is an increase on temperature as reaction proceeds, reaching a maximum, followed by a decrement. The increase in temperature is due to the highly exothermic polymerization reaction, but as monomer is consumed by the reaction, temperature decreases. All of the cuttlebone filled cements show lower peak temperature than the non filled cement (Figure 1), and peak temperatures are smaller than the maximum temperature allowed by Norm ISO 5833[12] (90 °C). Moreover, as the content of cuttlebone increases, peak temperature decreases and the time to reach the peak temperature increases, denoting a slower reaction. A decrease in peak temperature and slower reaction has also been reported when using HA as a filler.[8] Because a lower temperature peak may cause less damage to surrounding tissues, lower reaction rates are convenient for long term fixation of an implant. The slower reactions and peak temperatures can be explained in terms of filler higher thermal conductivity ($2.4 \sim 3.0\ W/m \cdot K$) compared to that of PMMA (0.46 W/mK).[14] For those reasons, generated heat can be dissipated more rapidly at the air cement interface. Peak temperature decreases more when using particles with smaller size, because there is faster heat dissipation by the particles due to the total higher contact surface area.

Table 1 shows that setting time increases with filler content. It may be beneficial to have enough manipulation time before the cement sets. However, if setting time is too large, medical problems can arise because pressure in the prosthesis has to be maintained until the cement sets. However, setting time can be adjusted by modifying the accelerator concentration. Using HA as filler for acrylic cements, setting times between 1.6 to 9.0 minutes have been reported.[15]

Table 1.
Identification code, maximum reaction temperature, setting time and residual monomer of poly (methyl methacrylate-*co*-styrene) cements filled with cuttlebone.

Variable Code	Filler (wt %)			Maximum Temperature (°C)	Setting Time (min)	Residual Monomer (wt %)	K_{ic} (MPa * m1/2)
	Sieve 270	Sieve 400	Sieve >400				
P00	–	–	–	59.2 ± 1.8	2.1 ± 0.3	4.6	1.37 ± 0.13
P10270	10	–	–	56.6 ± 0.8	3.2 ± 0.2	4.9	1.29 ± 0.04
P30270	30	–	–	53.1 ± 1.4	3.5 ± 0.2	4.6	1.11 ± 0.03
P50270	50	–	–	44.1 ± 1.4	2.6 ± 0.2	4.7	1.23 ± 0.11
P10400	–	10	–	55.6 ± 1.6	4.1 ± 0.1	5.1	1.14 ± 0.08
P30400	–	30	–	51.6 ± 2.1	5.0 ± 0.2	5.1	1.03 ± 0.15
P50400	–	50	–	49.1 ± 1.5	3.3 ± 0.1	5.3	0.89 ± 0.06
P10>400	–	–	10	54.7 ± 0.7	6.5 ± 0.2	5.5	0.70 ± 0.06
P30>400	–	–	30	46.0 ± 4.3	6.8 ± 0.4	5.9	0.59 ± 0.09
P50>400	–		50	48.6 ± 3.3	6.2 ± 0.6	6.0	0.70 ± 0.05

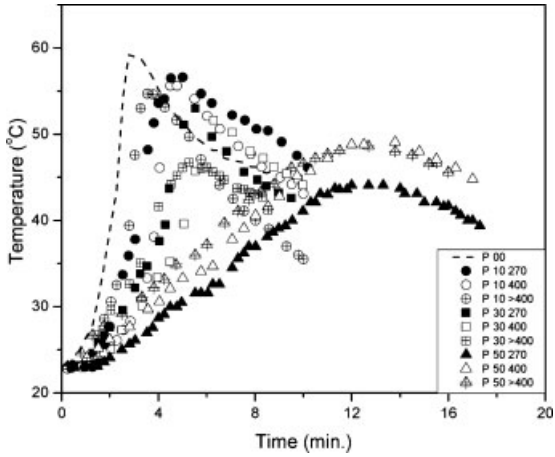

Figure 1.
Evolution of temperature as a function of reaction time for composites using different particle size and particle concentration.

Residual monomer content was determined by NMR 24 hours after cement curing. In Table 1, it can be observed that increasing the amount of filler, the amount of residual monomer increases because of lower monomer diffusion rate to reaction sites, due to the lower temperatures throughout the reaction (Figure 1).

Figure 2 shows that Young's modulus of the filled cements is higher than that of the unfilled cement. Young's modulus increases when increasing cuttlebone content from 10 to 30 wt %. This is in agreement with the increase in Young's modulus that has been reported for acrylic cements filled with hydroxyapatite.[16] However, such direct dependence was not accomplished for particles smaller than 53 μm when using 50 wt %. of filler. With that filler concentration, Young's modulus decreased with the exception of the composite prepared with the biggest particle size. The static modulus decrease can be explained by the occurrence of mixing difficulties when using particles with the smaller sizes, which in turn cause a larger amount of voids.[7,17]

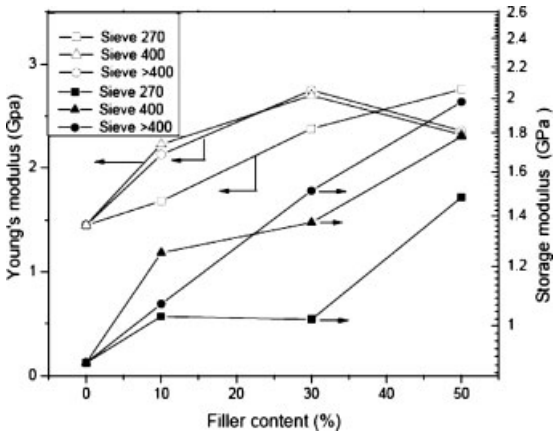

Figure 2.
Youngs and storage moduli of composites as a function of particle size and concentration.

Nevertheless, it can also be seen in Figure 2, that a direct response of storage modulus (measured at 40 °C) was attained for the

two composites considered for dynamic measurements. Such response of a variable which is in direct relationship with Young's modulus,[18] indicates that if a cyclic low deformation in torsion is used, the voids influence in material response is diminished.

A typical mechanodynamic response as a function of temperature for the composites prepared in this work can be observed in Figure 3. There, in the 30–50 °C range, the composites show a direct dependence with filler content maintaining a high storage modulus value. Then, as temperature increases storage values start to decrease rapidly. That means, that the composites are able to sustain their properties within the necessary temperature range (up to 50 °C) for arthroplasty applications.

Figure 4 shows that cements containing 10 wt % of cuttlebone filler, exhibit an ultimate strength slightly higher than that of the non filled cement. However, at higher filler concentrations, that value decreases. For the cements containing 10 and 30 wt % of filler, ultimate strength, within experimental error, presents small variation concerning to particle size. The decrease in ultimate strength beyond 10 wt % of filler can be explained in terms of pore formation, which weakens the composite as deformation increases. It has been reported that the addition of HA promotes cement porosity causing a decrease in tensile and compression strength.[7,17]

Figure 5 and 6 show that the presence of filler produces a decrease in bending modulus and bending strength as the cuttlebone concentration is increased. This decrease can be explained also by mixing difficulties as the amount of filler increases which causes particle agglomeration and voids, filler clusters represent weak points for the composite when stress is applied. It has been reported a decrease in bending strength when using HA as filler[6,16] Nevertheless, all the cements comply with the minimum value for bending modulus (1.8 GPa) and with the exception of the cement filled with 50 wt % of cuttlebone, the composites presented a bending strength higher than the minimum required (50 MPa, ISO-5833).[12] Particle size seems not to affect greatly bending modulus and bending strength for concentrations up to 30%.

Figure 7 shows that compressive strength decreases by the presence of cuttlebone particles and, that this decrease is higher as particle concentration is increased. A decrease in compressive strength has been reported when using HA as a filler due to

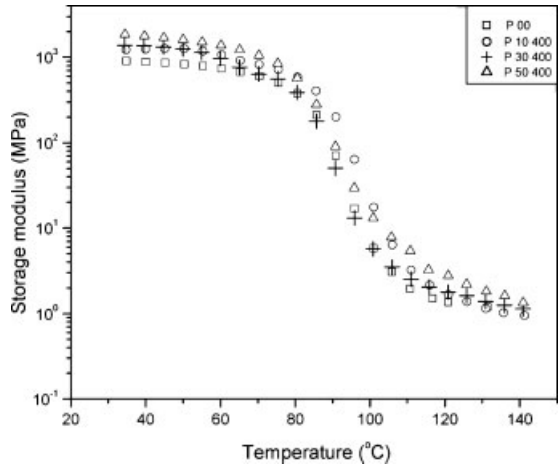

Figure 3.
Storage modulus as a function of temperature for composites prepared varying filler content.

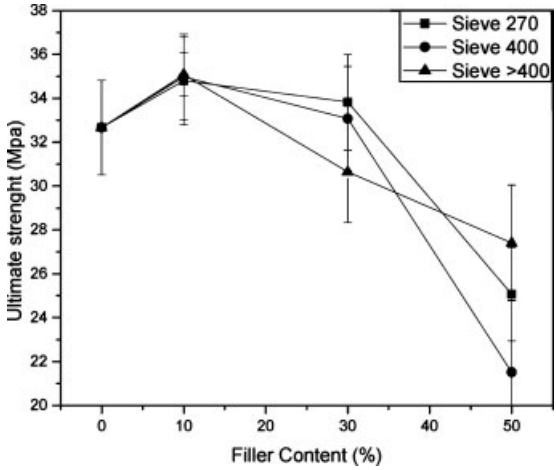

Figure 4.
Ultimate strength as a function of particle size and concentration.

cluster formation.[6] However, the formulations studied here present a value higher than the minimum required (70 MPa).[12] The reduction in compressive strength values can be explained also by particle agglomeration and void formation, due to the higher viscosity of the mixture as the amount of filler particles is increased. Particle size seems not to affect greatly compressive strength.

Fracture toughness (K_{Ic}) for the cement compositions studied here are included in Table 1. There, it can be seen that incorporation of cuttlebone filler to the matrix, causes a decrease in K_{Ic} value, and as the amount of filler concentration increases such decrement is higher. Also a small decrease in K_{Ic} is observed as particle size decreases. The decrease in K_{Ic} can also be explained in terms of the voids formed by the trapped air when mixing cuttlebone particles with cement formulations. Higher filler content or smaller particle size produces a higher viscosity

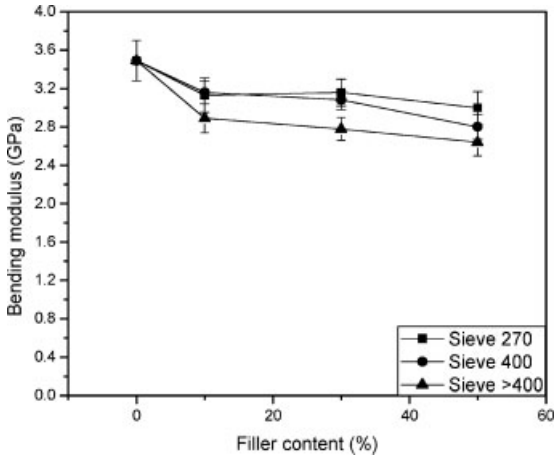

Figure 5.
Bending modulus as a function of particle size and concentration.

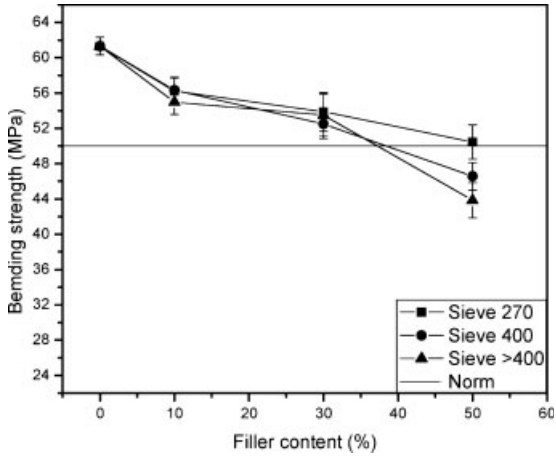

Figure 6.
Bending strength as a function of particle size and concentration.

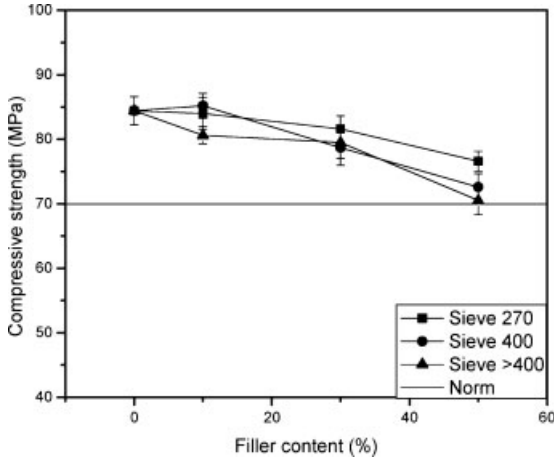

Figure 7.
Compressive strength as a function of particle size and concentration.

mixture and more air can be trapped.[7,17] Nevertheless, filled cements containing 10 and 30 wt % of cuttlebone filler, have a K_{Ic} within the reported values for commercial cements (0.88–1.5 $MPa \cdot m^{1/2}$).[19]

Conclusions

The cuttlebone filled cements present lower peak temperature than the non filled cement, and such value decrease as cuttlebone content is increased. Decreasing particle size causes a lower peak temperature.

The presence of cuttlebone particles as filler modified the mechanical properties of the acrylic cement; nevertheless, it is important to notice that for the composites containing up to 30 wt % of cuttlebone particles, bending modulus, bending strength and compressive strength are within the accepted values for bone cements and

present K_{Ic} values similar to the commercial ones. In general, for the studied ranges, filler concentration is more critical than particle size for mechanical performance.

The mechanical functionality of bone cements filled with cuttlebone particles at concentrations of 10 and 30 wt %, combined with the already proven osteointegration, makes this composite a good prospect for cement arthroplasty.

[1] G. Lewis, J. Biomed, *Mater. Res. Part B, Appl. Biomater.* **2008**, *84*, 2.
[2] S. M. Kenny, M. J. Buggy, *Mater. Sci. Mater. Med.* **2003**, *14*, 923.
[3] D. J. Berry, W. S. Harmsen, D. M. J. Ilstrup, *Bone Joint Surg.* **1998**, *80-A*, 1632.
[4] L. S. Toksvig, H. Franzen, L. H. Ryd, *Acta Orthop. Scand.* **1991**, *62*, 102.
[5] C. R. Leeson, T. S. Leeson, A. A. Paparo, *Tex/Atlas of Histogy*, ed. Elsevier, **1988**.
[6] S. Y. Kwon, Y. S. Kim, Y. K. Woo, S. S. Kim, J. B. J. Park, *Biomed. Mater. Eng.* **1997**, *7*, 129.
[7] C. I. Vallo, P. E. Montemartini, M. A. Fanovich, L. J. M. Porto, T. R. J. Cuadrado, *J. Biomed. Mater. Res. (Appl. Biomater.)* **1999**, *48*, 150.
[8] L. Morejón, E. Mendizábal, C. F. Jasso, J. A. Delgado, E. H. Barbosa, N. Davidenko, *Inter. J. Polym. Mater.* **2003**, *52*, 637.
[9] S. Shinzato, T. Nakamura, T. Kokubo, Y. Kitamura, *J. Biomed. Mater. Res.* **2001**, *56*(4), 571.
[10] S. Enriquez, H. E. R. Guadarrama, I. Reyes- González, E. Mendizábal, C. F. Jasso-Gastinel, B. García-Enriquez, D. Rembao-Bojórquez, C. Pane-Pianese, *J. of Biomat. Sci.: Polym. Ed.*, in press.
[11] ASTM D 638-1991. Standard Method for Tensile Properties of Plastics **1991**.
[12] ISO 5833-2002. International Standard, Implants for Surgery-Acrylic resin cements. **2002**.
[13] ASTM D5045-99 Standard Test Methods for Plane-Strain Fracture Toughness and Strain Energy Release Rate of Plastics Materials **1999**.
[14] CRC "*Handbook of Chemistry and Physics*", David R. Lide, Ed., CRC Press, 87th ed., **2006–2007**.
[15] A. Canul-Chuil,, R. Vargas-Coronado, J. V. Cauich-Rodriguez, A. Martinez-Richa, E. Fernandez, S. N. Nazhat, *J. Biomed. Mater. Res. Part B, Appl. Biomater.* **2003**, *64*(1), 27.
[16] K. T. Chu, Y. Oshida, E. B. Hanckok, M. J. Kowolik, T. Barco, S. L. Zunt, *Bio. Med. Mater. Eng.* **2004**, *14*, 87.
[17] Y. S. Kim, Y. H. Kang, J. K. Kim, J. B. Park, *Bio. Med. Mater. Eng.* **1994**, *4*, 37.
[18] J. D. Ferry, *Viscoelatic Properties of Polymers*, Ch.1, Third Edition, John Wiley&Sons, New York 1980.
[19] G. Lewis, J. Nyman, H. H. Trieu, *Biomaterials* **1998**, *19*, 96.

