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Mechanical and Thermal Properties of Hydroxyapatite-Impregnated Bone Cement

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Abstract: Self-curing acrylic cements, consisting mainly of polymethylmethacrylate (PMMA), are widely used in dentistry and orthopedic surgery. One of the major side effects of the standard PMMA application is tissue necrosis at the bone-cement interface due to the rise of temperature during the polymerization reaction. This may also lead to aseptic loosening over time. Therefore, intense research is being carried out in the development of bone cements with new compositions. In this study, the aim was to develop new bone cement compositions that would have low setting temperature and high mechanical strength and be comparable with the commercially available ones. For this purpose, PMMA bone cements having various amounts of hydroxyapatite were prepared. In order to obtain a proper and homogeneous distribution of hydroxyapatite particles within the cement, very low-viscosity PMMA bone-cement compositions were developed. The addition of hydroxyapatite decreased the polymerization temperature (from 111°C to 87°C) and increased the compressive strength (from 110 MPa to 122 MPa) of the resultant cements. These new bone cements have setting temperatures and mechanical strengths comparable with commercially available cements and are believed to be more biocompatible since hydroxyapatite is a natural mineral present in the bone structure.

Key Words: PMMA, bone cement, biomechanics, hydroxyapatite, biocompatible

Introduction

Acrylic bone cements mainly consist of polymethylmethacrylate (PMMA), and have been used in orthopedic surgery and in dentistry for more than forty years [1-3]. In orthopedic surgery, bone cement serves as a mechanical interlock between the metallic prosthesis and the bone, and it is found to be an appropriate material to transfer the load homogeneously [2,4].

Bone cements are generally prepared from two components: a powder and a liquid. The powder consists of PMMA microspheres (10-150 microns) and a polymerization initiator, usually benzoyl peroxide (BPO). The liquid part consists of methylmethacrylate (MMA) monomer and a polymerization accelerator, usually N,N-dimethylparatoluidine (DMPT) [2,3]. Prior to the application, the powder and the liquid parts are mixed for 4-8 minutes until a soft dough is obtained and then applied to the desired bone cavity. Because of a rapid polymerization reaction, bone cement hardens in the following 3-5 minutes.

The main adverse effect of bone cement application is a rise in temperature at the bone and cement interface during the exothermic polymerization reaction [1-3, 5]. Maximum temperatures in the range of 80°C to 124°C have been reported [1,3,5,6]. These values are at least 50% higher than the limit for thermal damage to living tissue (48 - 60 °C) [6]. Furthermore, the monomer that may be released from the cement structure causes a severe drop in blood pressure during surgery, and the monomer is itself toxic. Both factors, the exothermic

reaction and the presence of the liquid monomer, leave a thin gap between the bone and the bone cement, which leads to aseptic loosening [4].

In earlier studies carried out to design new compositions (in order to decrease the curing temperature, improve the mechanical properties, and solve the loosening problem), the effects of molecular structures of the polymer and monomer and/or the presence of mineral particles in the cement compositions were examined [5-8]. Hydroxyapatite (HA) is a suitable mineral for use in the reinforcement of organic-based cements in terms of mechanical and biological properties. HA is known to be biocompatible, osteoconductive and osteophilic. It has been reported that the addition of HA to bone cements improves their biological properties as well as increasing their strength [9]. In the presence of HA particles, ingrowth of bone forming cells, bone formation and enhanced bonding between bone and cement have been observed [10, 11].

There are also some contradictory reports stating that the addition of hydroxyapatite decreased mechanical strength [1] and that variation in molecular structure caused early cement failure [8]. In order to improve the mechanical properties of the cements, other additives such as carbon fibers [12,13], self-reinforced PMMA fibers [14,15] and Kevlar29® aramid fibers were introduced [2,13,16]. Also, the effect of composition on the mechanical properties was studied by using various monomer combinations, such as a mixture of hydroxyethylmethacrylate (HEMA) and ethyleneglycol dimethacrylate (EGDMA) [1] or silane-treated hydroxyapatite containing polyethylmethacrylate and n-butylmethacrylate compositions [17].

The aim of this study was to prepare acrylate bone cements with new compositions that have lower curing temperatures and better mechanical properties. For this reason, ground PMMA particles of different molecular weights were used and various compositions with different polymer-to-monomer ratios were prepared. The influence of hydroxyapatite filler on the polymerization temperature, compressive strength, handling and flow characteristics of the bone cement was examined.

Materials and Methods

Materials

Methyl methacrylate monomer (MMA) was purchased from Merck A.G. (Germany). Polymethylmethacrylate (PMMA, Av.MW. 120000 and Av.MW. 15000), Benzoyl peroxide (BPO) and N,N-dimethyl paratoluidine (DMPT) were obtained from Aldrich Chemical Co. Inc. (USA). Hydroxyapatite (HA) was purchased from Riedel-de Haën A.G. (Germany). CMW1 and CMW3 bone cements were provided by Hipokrat A.Ş. (Turkey).

Preparation of Polymers

Commercially obtained PMMA particles were ground and sieved through a 150- micron mesh. The average size and the size distribution curves were obtained by Malvern Mastersizer, particle size analyzer (Malvern Instruments Ltd., UK).

The powder component of the bone cements was prepared by mixing sieved PMMA and BPO (1.1%, w/w). In some compositions, HA was added to the mixture. The liquid component was prepared by mixing MMA (2.0 g = 2.12 mL) and DMPT (0.85% v/v, 18 microliter). CMW1 and CMW3 bone cements were used as references. All the samples were kept in a constant temperature room (23 ± 1°C) for at least two hours to achieve thermal equilibrium prior to each experiment. For cement preparations, two parts powder and one part liquid were intensively mixed and used in further tests. The compositions used are presented in Table 1. The powder and liquid compositions of CMW1 and CMW3 bone cements are presented in Table 2.

Table 1. Compositions of cements

	POWDER				LIQUID	
Sample	PMMA(g) (MW=120000)	PMMA(g) (MW=150000)	BPO (mg)	Hydroxyapatite (g)	MMA (g)	DMPT (uL)
C0	3.0	1.0	45	0.0	2.0	18
C1	3.0	1.0	45	0.5	2.0	18
C2	3.0	1.0	45	1.0	2.0	18
A0	2.0	2.0	45	0.0	2.0	18

Table 2. Powder and liquid compositions of CMW1 and CMW3.

	POWDER						LIQUID	
	PMMA*	BaSO4*	BPO*	MMA*	DMPT*	HQ*	Ethanol*	AA*
CMW1	88.3%	9.1%	2.6%	98.66%	0.40%	15-20 ppm	0.92%	0.02%
CMW3	87.8%	10.0%	2.2%	98.07%	0.99%	15-20 ppm	0.92%	0.02%

*PMMA, polymethylmethacrylate; BaSO4, bariumsulphate as radiopaque; BPO, benzoylperoxide; MMA, methylmethacrylate; HQ, hydroquinone; AA, ascorbic acid.

Thermal and mechanical experiments were performed on four different compositions and CMW bone cements and for each set at least five samples were examined. All experiments were performed at 23±1°C room temperature.

Temperature Measurements

J-type thermocouple wires were purchased from Elimco Co. (Turkey). Thermocouple wires, composed of two side-by-side dissimilar alloy metals, were cut into equal pieces of 5 cm. Isolators of every small piece were removed and one end was electrically welded. The welded end formed a thermocouple junction. In the polymerization temperature measurement process, an Omega data acquisition device (Omega Engineering Inc., USA) was used. One end of the thermocouple was connected by a dual-line cable to the Omega, which was controlled by a computer, and the other end of the thermocouple was used as a temperature sensor.

To measure the curing temperature, powder and liquid components were mixed for 90 seconds, kneaded by hand for 1-2 minutes and molded into a spherical shape, and the thermocouple was inserted in the center of the dough. Temperatures were recorded for 1200 seconds in each experiment. For each composition at least five specimens were prepared and subjected to thermal tests.

Mechanical Testing

The molds used in the preparation of compressive mechanical test samples were made of three stainless steel cylindrical plates 76 mm in diameter and 12 mm in height. One of the plates was perforated and had 6 mm-diameter cylindrical holes (Standard Specification for Acrylic Bone Cement, ASTM Designation F451-95).

The powder and liquid parts of the cements were mixed for 90 seconds. Six grams of dough was put on the perforated plate and pressed by the other two plates on both sides. The three plates were held together tightly for 1 h by a C-clamp. After that the mold was dismantled, and the ends of the hardened rods were polished by abrasion on sand paper and washing with water. After surfacing, the specimens were removed from the mold. Each specimen was examined visually for physical imperfections resulting from molding operations. Specimens with defects or pores that occupied more than 10% of the cross-sectional area of the specimens were discarded. The cylindrical specimens, were kept in saline solution at 37°C for 24h and then were subjected to compression tests at a loading speed of one inch per minute. Compression tests were performed in a Lloyd® M50K mechanical testing machine (Lloyd Instruments Limited, UK). For each composition at least five specimens were tested.

One-way ANOVA was used to determine the significance of the differences of the thermal and mechanical properties of the prepared compositions.

Results

Particle size analysis:

The average size of the PMMA particles was about 95 µm and about 50% of the particles were below this size. According to the data obtained computer, 10% of the particles were below 39 µm and 10% were above 154 µm. The size distribution curve is given in Figure 1.

Cement preparation:

The cement mixture prepared from PMMA particles with Av.MW.120000 had high viscosity, and therefore the cement dough was not soft enough for handling, mixing, working and application. In clinical practice, the cement must flow into the cancellous bone as pressure is applied. If the viscosity of the dough is too high, the

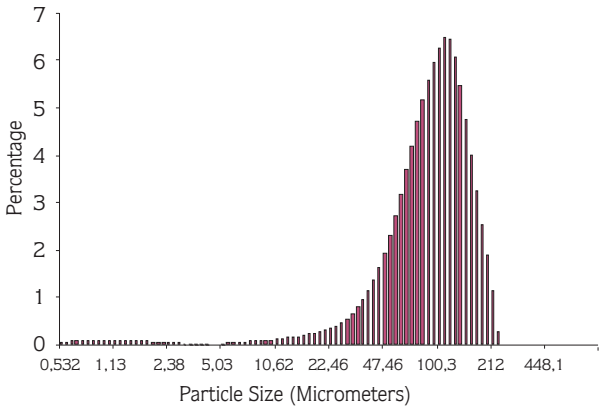

Figure 1. Particle size distribution of PMMA particles

intrusion into bone interstitial trabeculae is poor, and that prevents good mechanical coupling between the bone and the cement. Thus, in this study, a certain amount of low molecular weight PMMA (Av.MW.15000) was added to the mixture in order to decrease the viscosity of the starting composition. The addition of low molecular weight PMMA increased the flow quality of the cement dough, but further additions caused an extreme decrease in viscosity, eventually leading to a cement with low compressive strength. Those samples became brittle, and crack propagation after solidification was facilitated. This kind of backdrop was observed for A0 samples, as shown in Figure 2. Therefore, it was decided that the ratio of low molecular weight PMMA to high molecular weight PMMA should be 1:3 and this ratio was kept constant (with or without hydroxyapatite) throughout the experiments.

HA was added at certain ratios that led to workable and applicable dough. Again, further additions of HA

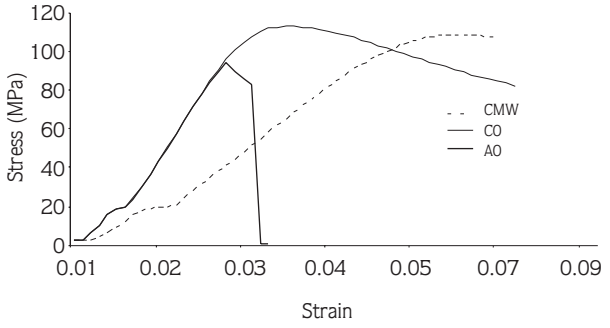

Figure 2. Compressive stress/strain graphs of three different compositions.

(1g/4g mixture) caused very viscous unmanageable dough.

Curing temperature:

For the samples that were prepared in C0 compositions, the maximum temperature observed was 111±1.0°C, and this peak temperature was observed 530 seconds after mixing the solid and the liquid components. For samples C1 and C2, the maximum temperatures were recorded as 103±1.0°C and 87±1.0°C, respectively. These maximum values were obtained in about 400 seconds and 470 seconds, respectively. The temperature changes of these samples over time are shown in Figure 3. The decrease of the

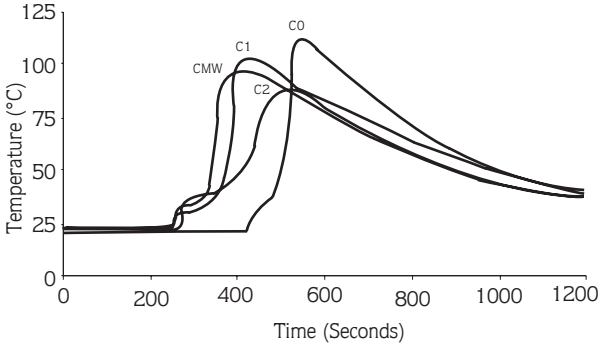

Figure 3. Polymerization Temperatures of Bone Cements.

temperature from 111°C to 87°C was caused by the presence of HA in the mixture ($p<0.001$). This could be explained by the presence of a solid material that is homogeneously distributed in the cement dough and is able to absorb some of the heat evolved in the exothermic reaction of polymerization, causing a decrease in the temperature of the medium. However, the HA content could not be further increased because it could cause hardness and difficulty in mixing and processing of the cement dough, as well as imperfections as a result of aggregation of HA particles.

Mechanical properties:

Surgical PMMA cement is brittle in nature. Like all brittle materials, it is weak under tension but quite strong in compression, and is capable of yielding under uniaxial compression. Therefore, the yield strength was determined in compression. Another reason for this

choice is that the main direction of load on bone cement in a total hip implant is compression.

It was observed that HA addition caused an increase in the compressive strength of the samples prepared. The compressive strengths of the bone cements increased by about 10%, from 110±2.2 MPa to 122±2.8 MPa with the introduction of 8% HA ($p<0.001$). Further addition of HA (up to 14%) decreased compressive strength by about 4% (down to 105±4.4 MPa) ($p<0.001$) (Table 3, Figures 4, 5). This is in accordance with the reports that state that the addition of hydroxyapatite without any chemical treatment decreased the mechanical strength of the bone cement [18]. One factor that may help to explain the observed compressive behavior is the degree of adhesion between the HA particles and the matrix. In a heterogeneous solid solution, poor adhesion between the components causes a decrease in yield stress as if the system were filled with voids. HA microparticles behave as load carriers, leading to good mechanical properties if they are present in small amounts and distributed homogeneously in the cement dough. If the proportion of the HA particles increases, this could lead to non-homogeneous distribution and, therefore, aggregation of particles may occur. This may cause phase segregation, inhomogeneity in the structure and poor adhesion to the matrix, leading to a decrease in the compressive strength.

Table 3 and Figures 4 and 5 show the combined results of the effect of HA on curing temperature and compressive strength. C0 samples, which did not contain any HA, had very low viscosity, poor processing

	CMW	C0	C1	C2	A0
Ultimate Compressive Strength (MPa)	110±2.3 n=9	110±2.2 n=5	122±2.8 n=5	105±7.4 n=5	95.6±9.3 n=5
Compressive Elastic Modulus (GPa)	2.26±0.04 n=9	2.32±0.05 n=5	2.40±0.20 n=5	2.57±0.30 n=5	2.22±0.10 n=5
Maximum Curing Temperature(°C)	96±0.9 n=9	111±1.2 n=5	103±1.0 n=5	87±0.9 n=5	95±0.9 n=5

Table 3. Mechanical and thermal properties of the bone cements.

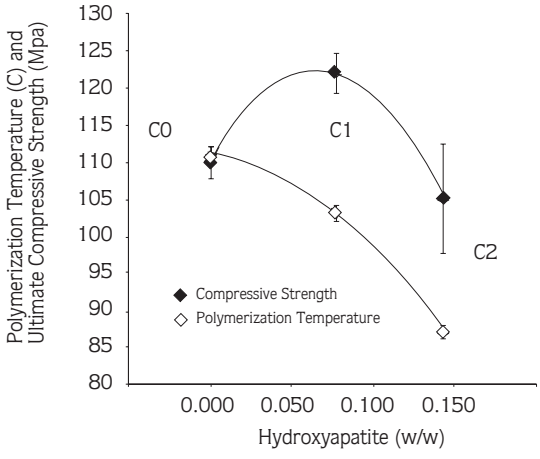

Figure 4. Change of Ultimate Compressive Strength and Maximum Curing Temperature due to Hydroxyapatite Content with Fitted Theoretical Curves.

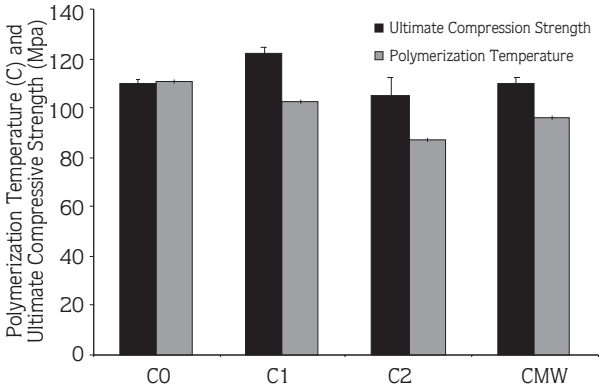

Figure 5. Ultimate Compressive Strength and Maximum Curing Temperatures of various cements

properties and high setting temperatures. For C1 samples, the content of HA in the total bone cement was 0.5 g and for C2 samples it was 1.0 g. These values were about 8% and 14% of the total weight of the cement mixture, respectively. If both effects are considered, the addition of HA causes a continuous decrease in curing temperature, which is a desired property, and gives a maximum compressive strength of about 8%, which is also a desired property. When both of these properties are considered, the optimum composition seems to be the one which contains about 10% HA. This composition will have a lower curing temperature and a higher compressive strength than the original.

Compressive elastic modulus values are given in Table 3 and Figure 6. The change of compressive elastic modulus, from 2.32 to 2.57 GPa with addition of 14 % HA, was not significant ($p<0.2$).

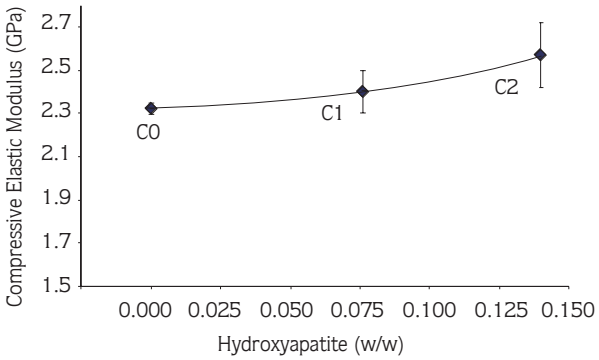

Figure 6. Change of Compressive Elastic Modulus with Hydroxyapatite.

Conclusion

The success of the implant fixation is associated with the mechanical interlock between the cancellous bone and the cement, and this depends on the viscosity of the initial dough. In this study, initially a very low -viscosity bone-cement composition was prepared. For this sample (C0) the setting time was quite long (ca. 530 seconds) and the setting temperature was quite high (111ºC). Compressive strength was the same as that of the commercially available CMW cements (ca. 110 MPa). HA was added to this composition and its effects on setting temperature, compressive strength and hardness were examined. Since the viscosity was very low, the mixing process was quite easy and homogeneous samples were obtained. However, the addition of high amounts of HA (higher than 14%) caused a decrease in the 'flow' characteristics of the dough. Therefore, studies were carried out with samples containing a maximum of 14% HA. On the other hand, the addition of high amounts of HA caused a decrease in the compressive strength of the cements possibly due to phase segregation. In other words, HA begins to aggregate behaving like voids in bone cement and decreasing the mechanical strength.

The ultimate aim of this study was to develop a bone cement with low exothermicity without compromising the mechanical properties so that the greatest disadvantage of cemented hip replacement is avoided. When the data obtained for the bone cement formulations developed and those of the commercial product CMW are compared it is observed that composition C2, which contains 14% HAP, has a substantially lower temperature (87°C vs 96°C) while the mechanical properties (ultimate compressive strengths and compressive elastic moduli) are comparable.

Although maximum strength was obtained for samples containing 8% HA, the curing temperatures of commercial bone cements are theoretically achieved in samples containing 10% HA. Therefore, bone cement compositions containing 10% HA are recommended.

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