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Properties of PMMA Bone Cement Modified with Nano-hydroxyapatite and Acetone

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Abstract

Fracture in the adjacent levels is one of the consequences to the use of commercial poly methylmethacrylate (PMMA) bone cement. Modified PMMA with a reduced Young's modulus was found to be safer for cancellous bone augmentation procedures. The aim of this research was to study the effect of adding hydroxyapatite (HA) nano-particles and acetone on different properties of PMMA cement. A commercial PMMA cement was used as a model for bone cement. Three groups of modified PMMA/nano-HA were investigated by adding 2, 4 and 6 wt. % of HA. Acetone as a porogen mixed with distilled water in different amounts (A/W: 1:1, 2:1.5 and 2:1g) was used to produce porous PMMA cement. The residual monomer, polymerization and mechanical properties under tension and compression tests were investigated. Young's modulus detected from compression test decreased from 826.5±10 to 728±66 MPa by adding 6wt.% HA. Adding acetone to PMMA with 2:1.5g (A/W) has decreased the compressive Young's modulus to 753±38 MPa. High Performance Liquid Chromatography (HPLC) measurements were carried out with intervals of 2 hours, 6 hours and 24 hours to evaluate the residual monomer for all groups. The amount of residual monomer has decreased after 24 hours of curing by adding acetone and nano-HA. Modifying PMMA by HA and acetone have inconsistent effect on the polymerization temperature. It was concluded that HA and acetone can be used to reduce the stiffness and residual monomer with enhanced biocompatibility of the commercial PMMA bone cement.

Keywords

Poly methylmethacrylate ; acetone; hydroxyapatite; adjacent fracture; residual monomer; stiffness.

1. Introduction

Osteoporotic vertebral fracture is one of the major health problems that can cause a lot of pain, kyphotic deformity and decreased life quality. Recently, there is an increase of using Vertebroplasty to treat these fractures. Vertebroplasty is a minimally invasive technique that involves percutaneous injection of PMMA bone cement into a weakened or fractured vertebra in order to strengthen and stabilize it [1]. The mechanical objective of Vertebroplasty is to restore the structural properties of the weakened vertebrae to its normal values, so that the weight-bearing kinetics during regular daily activities is sufficiently supported [2]. The commercially available PMMA bone cement has a Young's modulus (Stiffness) in the range of (2–3 GPa) [3]. These values are 4–40 times higher than that of cancellous bone (50–800 MPa) which is the main constituent of the vertebral body. An increased fracture risk has been demonstrated for the adjacent vertebral bodies after augmentation. The inherent high stiffness of the PMMA

is hypothesized to be the main reason for these adjacent fractures [4]. Moreover, PMMA has other disadvantages such thermal necrosis due to the exothermic polymerization reaction. The PMMA polymerization temperature may increase up to 70 ^{o}C during setting inside the vertebral body which can result in heat damage of the neighboring healthy tissues [4, 5]. Chemical necrosis due to the monomer release is one of the PMMA disadvantages as well. Researchers have tried to hinder these limitations by using different additives [6-10]. Adding biocompatible synthetic bone substitutes such as hydroxyapatite (HA) and α-TCP powders has shown enhanced mechanical properties and biocompatibility of the PMMA bone cement [6-9]. Introducing internal porosity is another approach to modify PMMA bone cements [11-13]. Internal porosity can decrease the injurious high stiffness of PMMA bone cement and enhance its biocompatibility as it allows bone tissue ingrowth [13]. The aim of this research work is to study the effect of adding nano-HA powder and acetone to the PMMA bone cement in order to hinder its limitations. The effect of adding nano-HA and a biocompatible porous agent (porogen), namely acetone, on the mechanical properties, polymerization temperature and monomer release will be addressed. Acetone is the main precursor in the manufacturing of MMA. It is a colorless liquid with a distinct odor that mixes readily with water. The supersaturated gas created by mixing water/acetone and the instant polymerization of PMMA can result in a porous structure [14]. Low levels of acetone normally exist in the human body from the breakdown of fat and is use in normal processes that make sugar and fat inside the body [15]. There is no strong evidence of chronic health effects on using acetone. Several studies show that there is no evidence of serious neurotoxic, neurobehavioral, or other pathological effects of acetone. Moreover, acetone was proven to be effective against some neurological disorders such as kindled focal seizures [16].

2. Materials and Methods

Materials

Effect of adding nano-HA powder:

[$(C_5O_2H_8)_n$] PMMA; Vertex; (Oldenbarneveltln, Netherlands), MMA; Vertex; (Oldenbarneveltln, Netherlands) was used as a model for bone cement. Nano-HA with average 200 nm was synthesized in home-laboratory as explained in previous research work (Biomedical Engineering laboratory, Mechanical Engineering Department, Al-Azhar University) [17].

Effect of Acetone/water amounts (A/W):

Acetone [C_3H_6O] (A0038111, EDWIC, Egypt), and Distilled water (Conductivity approx. 2.5 μS/cm) were used as a biocompatible porogen.

Preparation method

Effect of adding nano-HA powder:

HA-nano powder was added by various weight ratios 2%, 4% and 6% to the PMMA powder and hand mixed in a plastic cup with spatula. After powder mixing, the MMA was added to PMMA/nano-HA with a ratio equal to 2:3 and hand mixed for one minute. The mixture was cast in different sample molds for tension, compression, residual monomer and polymerization tmperature to characterize the different compositions.

Effect of Acetone/water amounts (A/W):

Acetone and water were blended with the following amounts: 1:1, 2:1 and 2:1.5 g (A/W). Then MMA and PMMA were blended with a ratio equal to 2:3 for one minute. The acetone/water blends were added to the PMMA and mixed for two minutes.

All samples in this research work were prepared in Biomedical Engineering laboratory; Mechanical Engineering Department; Al Azhar University. A factorial design 2 $\times$ 3 of two factors with three levels [A (nano-HA): 2, 4, 6 % and B (A/W): 1:1, 2:1 and 2:1.5 g] was applied with three repeats for each level in tension and compression testing. One repeat is used for thermal, polymerization and morphology testing

CHARACTERIZATION

Mechanical Testing

Tensile strength, compression strength, and modulus of elasticity of the modified PMMA model cement were determined by using universal testing machine (Zwick/Roell, Z010, Germany). Test procedure and dimensions of the specimens were according to ASTM 638 standard. Compression specimens were tested under the following parameters: Load cell: 10 kN, Pre-load: 5 N, Pre-load speed: 10 mm/min, and test speed: 5 mm/min. Tension specimens were tested by using 10 kN load cell and screw grip for specimen grips [18].

Maximum and setting Temperature

The thermal properties of PMMA cement modified by the different additives was studied according to European standard EN ISO 573-2:1996. A temperature sensor (Jenway 3510, England) was used. The temperature probe was placed in the mold cavity, approximately half way between the outer ring and the plunger [19]. The temperature of the PMMA cement increased with time due to the exothermic polymerization reaction. The temperature raising stops after polymerization process completed. The temperature of PMMA cement decreased with time until it reached room temperature. The temperature readings of the PMMA cement were recorded immediately after the placement of PMMA cement in the mold until it reached the room temperature every 60 seconds.

Monomer Release

High Pressure Liquid Chromatography (HPLC) (LC-2000 plus HPLC system, Jasco, Japan) was used to identify the residual MMA content according to the method described by Rca R B *et.al* [20]. The analysis used a Jasco UV detector at 230 nm, an Ace 5 C18 column, a binary pump, and manual injector system. Flow rate of the distilled water was 1 mL/min. Figure (1) shows the calibration curve constructed with an MMA concentration of 100 to 3000 ppm in acetonitrile. All of the specimens were stored in a glass flask, which was sealed with a leak-proof cap and tightly wrapped parafilm to avoid leakage. As an extraction solvent, 20 mL of methanol was added to the solution to precipitate the polymer. The specimens were maintained at 37 ^{o}C during the experiments (Fig. 1). To determine the release of the MMA over time, 20 µL of the extract samples solution were injected and analyzed by the HPLC at regular intervals. The time intervals were 2, 6 and 24 hours. The extracted solutions were evaluated to determine the rate of residual monomer release by comparing the area under the peak on the graph with that of standard MMA.

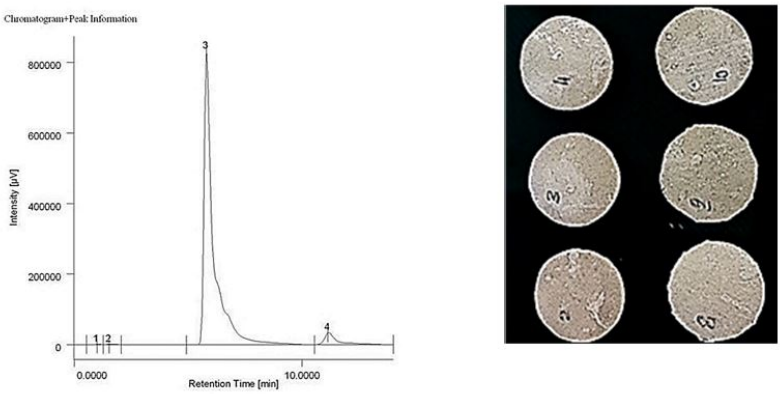

Figure 1. The calibration curve of standard MMA and samples of toxicity for vertexmaterials

3. Results

Mechanical Testing

Effect of nano-HA

Table 1 shows the mechanical properties of the modified PMMA/nano-HA cements that results from compression and tension testing. Increasing the amount of nano-HA affect the compressive stiffness and strength adversely.

The PMMA/6% nano-HA cement has the smallest compressive stiffness (728±66 MPa) and compressive strength (50.6±5.6 MPa). The nano-HA has a significant adverse effect on the elongation behaviour under tension. The lowest elongation (1.76 ±0.47 mm) was obtained for the PMMA/4% nano-HA cement. The same composition shows the lowest tensile stiffness and strength (504 ±88 and 16.9 ±7 MPa respectively) (Table 1).

Table 1. Mechanical properties of PMMA/nano-HA compositions

	Control	2% nano-HA	4% nano-HA	6% nano-HA
Tensile strength (MPa)	38.8 ±3	30.8 ±2	16.9 ±7	24.6 ±2.6
Tensile Young's modulus (MPa)	582 ±28	615 ±6	504 ±88	512 ±47
Elongation (mm)	3.5 ±0.26	2.67 ±0.09	1.76 ±0.47	2.46 ±0.11
Compressive strength (MPa)	66.8 ±2	72 ±7.5	62 ±1.8	50.6 ±5.6
Compressive young's modulus (MPa)	826.5 ± 10	971 ± 94	868 ±47	728 ±66

Effect of Acetone/water (A/W)

Various amounts of acetone and water were mixed with three levels and added to the PMMA model bone cement. Specifically, 1:1g, 2:1g and 2:1.5g (A/W) were added to 30g PMMA and 20g MMA (Table 2). Adding different amounts of A/W has decreased the strength, elongation and the Young's modulus under tension. The smallest tensile strength and tensile Young's modulus were 23.7±4.5 MPa and 529 ±57 MPa for the 2:1g (A/W) composition. However, the addition of A/W has increased the compressive Young's modulus except for the 2:1.5g (A/W) composition (753 ±38 MPa). The compressive strength has decreased with adding (A/W). The smallest compressive strength was recorded for the 2:1.5g (A/W) composition with 47.8 ±4.7 MPa (Table 2).

Table 2. Mechanical properties of PMMA-Acetone/Water (A/W) compositions

	Control	1:1g (A/W) 1	2:1g (A/W)	2:1.5g (A/W)
Tensile strength (MPa)	38.8 ± 3	38.7 ±1.9	23.7 ±4.5	26 ±0.9
Tensile Young's modulus (MPa)	582 ± 28	603 ±33	529 ±57	529 ±61
Elongation (mm)	3.5 ± 0.26	3.16 ±0.18	2.38 ±0.26	2.65 ±0.34
Compressive strength (MPa)	66.8 ± 2	64.8 ±3.3	65.9 ±1.4	47.8 ±4.7
Compressive young's modulus (MPa)	826.5± 10	902 ±49	933 ±47	753 ±38

Setting and maximum polymerization temperature

Effect of nano-HA

Figure (2) shows representative measurements of the cement polymerization temperature as a function of time after mixing of all PMMA/nano-HA compositions. Nano-HA has increased the polymerization temperature for all the composition. The maximum polymerization temperature was observed for PMMA-4% nano-HA with 41.4 ^{o}C and a setting temperature of 31.1 ^{o}C. The addition of 4% nano-HA has increased the setting time to 31 min.

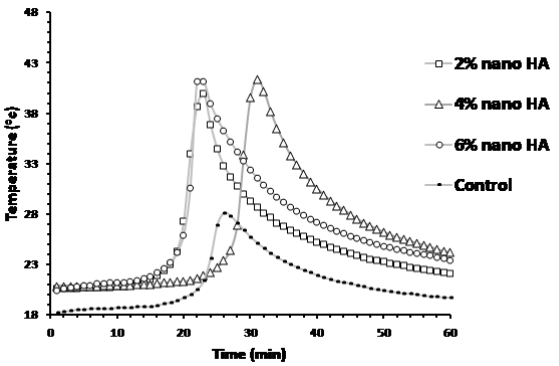

Figure 2. Representative polymerization temperature measurements for PMMA/nano-HA compositions as a function of time after start of mixing

Effect of Acetone/water (A/W)

Figure (3) represents the measurements of the cement temperature during polymerization as a function of time after start of mixing of different PMMA-(A/W) compositions. The addition of (A/W) amounts has decreased the setting time and increased the polymerization temperature. The maximum polymerization temperature was noticed for the 2:1 g (A/w) composition with 59.4 ^{o}C. The minimum setting time was observed for the 1:1 g (A/W) composition with 14 minutes after start of mixing (Fig. 3).

Monomer Release

The percentage of residual monomer by mass of all combinations after three different time intervals are represented in Table (3). According to the HPLC measurements, the residual monomer ranged from 0.027% to 0.45%. The (A/W) combinations shows a lower monomer release than that of the HA combinations after all time intervals. For all combinations and control group, the residual monomer started to decrease at 24h except for 2%nano-HA combination.

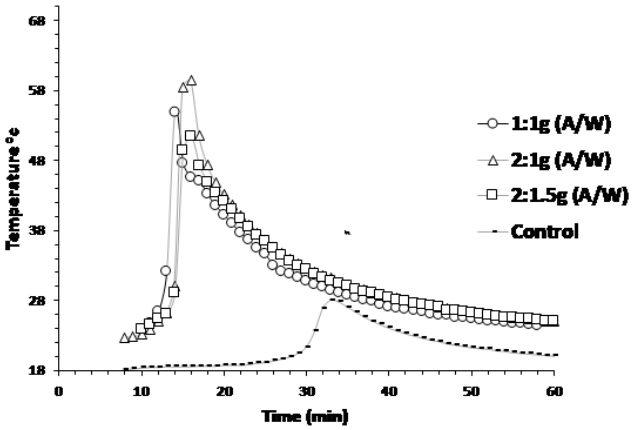

Figure 3. Representative polymerizationtemperature measurements for PMMA-(A/W) compositions as a function of timeafter start of mixing

Table 3. Table 1.Residual monomer content calculated as percentage of MMA by mass of thespecimens of all compositions after different time intervals

	2h	6h	24h
Control	0.094	0.214	0.095
2% nano-HA	0.095	0.180	0.450
4% nano-HA	0.093	0.225	0.186
6% nano-HA	0.086	0.226	0.218
1/1 g (A/W)	0.036	0.083	0.078
2/1.5 g (A/W)	0.028	0.061	0.053
2/1 g (A/W)	0.027	0.049	0.120

4. Discussion

To hinder the limitations of the PMMA bone cements, two approaches have been followed in this study. Nano-HA is added to PMMA to form a biocompatible composite. Mechanical properties are of the crucial characteristics of PMMA bone cement in the different biomedical applications. Mechanical characteristics under compression are dominant in specific applications such as vertebroplasty, kyphoplasty and vertebral augmentations. While, the mechanical properties under tension are dominant in other applications such as dental and arthroplasty. PMMA bone cement is a brittle material and therefore, it is weak in tension but quite strong under compression (Fig. 4). The inherent excessive stiffness (Young's modulus) under compression is hypothesised to contribute to adjacent frac-

tures in vertebral body augmentation. Therefore, the measurements of compression strength values of the prepared cements are very important in this research. Adding nano-HA to the PMMA can be considered as a dispersion reinforcement composites. The nano-HA size allows particle–matrix interactions to occur at the atomic or molecular level. Whereas the PMMA matrix bears the major portion of an applied load, the small dispersed nano-HA particles hinder the motion of dislocations. Thus, plastic deformation is restricted such that the compressive strength and stiffness increase as can be noticed in the 2% nano-HA combination (Table 1). The reinforcement effect depends on the uniformity of nano-HA distribution and its amount inside the matrix. The dispersion of nano-HA inside the PMMA matrix was quite a challenge and becomes a restraint with higher nano-HA percentage. Therefore, the reinforcement effect decreased to 728 $\pm$66 MPa for the 6% nano-HA combination (Table 1). Moreover, the poor adherence between the nano-HA particles and surrounding matrix could have a weakening effect that decrease strength and stiffness in tension and compression, with increasing the nano-HA percentage.

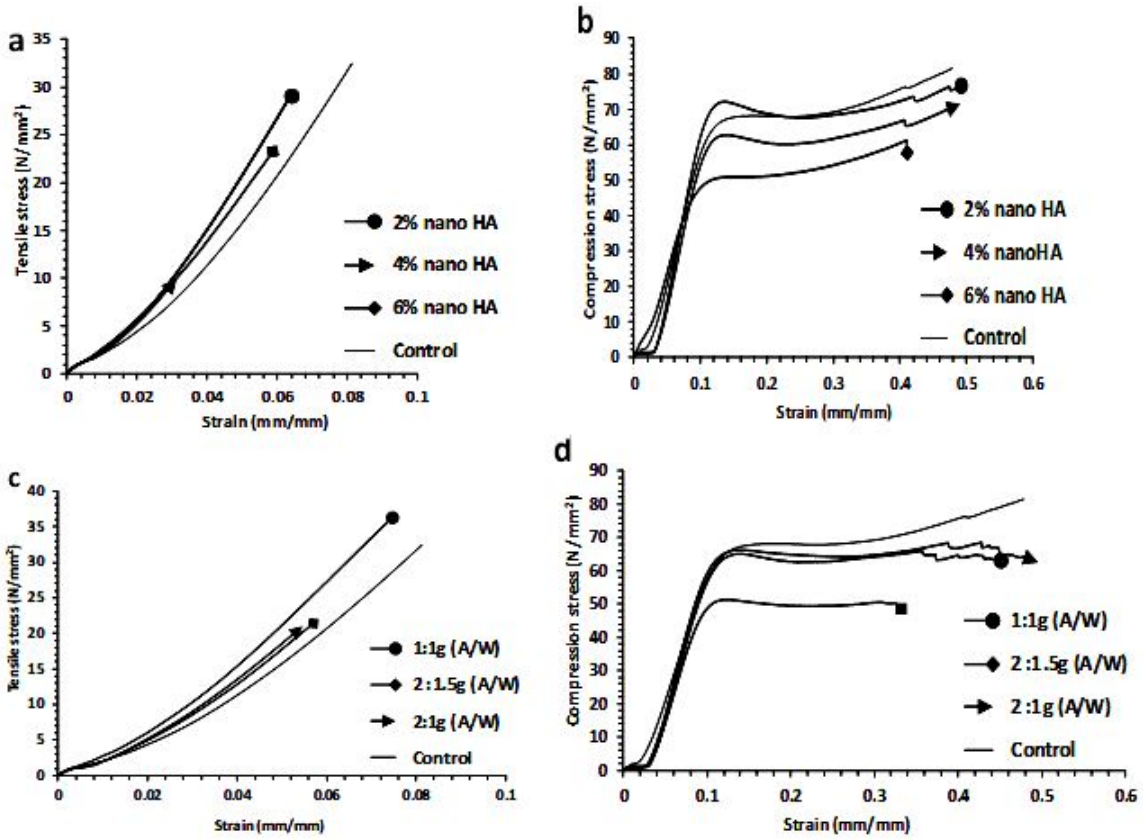

Figure 4. represents the tensile [a, c] and compression [b, d] curves for nano-HAand (A/W) combinations respectively

The second approach is to introduce porosity inside the PMMA cement by using acetone. Internal pores increase the opportunity of stress concentration and therefore decreases the maximum tensile strength. Different amounts of acetone and water were used as porogen when added to PMMA. Acetone has a lower polarity than water and a higher solubility than non-polar gases such as oxygen and nitrogen. When water and acetone are mixed together, gas solubility of the mixture decreased, thus allowing supersaturated Oxygen and Nitrogen gases to come out of the solution in the form of nanobubbles until the concentration is at the saturation level. These nanobubbles will produce porosity inside the PMMA and lead to reduction in weight and mechanical properties. Surprisingly, introducing porosity inside the PMMA matrix did not decrease the mechanical properties as accomplished by adding nano-HA (Tables 1 and 2). This could be correlated with polymerization temperature measurements [Figs 2 and 3]. Adding acetone contributes to high polymerization temperature. As the polymerization temperature increases, molecular mobility speeds up, leading to more complete polymerization. This increase in the polymerization temperature is found to be in the favor of enhanced mechanical properties but on the other hand it may increase the possibility of thermal necrosis. Despite of this thermal limitation of adding acetone, the complete polymeriza-

tion allows lower residual monomer percentage for all (A/W) combinations than that of nano-HA ones (Table 3). Therefore, the increase of residual monomer in the nano-HA combinations is deleterious to its mechanical properties.

5. Conclusions

Nano-HA as a ceramic bioactive phase can be used to reduce the stiffness, residual monomer and enhance the biocompatibility of the commercial PMMA bone cement. Yet, the Nano-HA agglomerated and produced non-adherence points inside the PMMA matrix. Acetone is a volatile biocompatible substance that can be used as an effective porogen to increase the porosity of the PMMA augmentation and consequently reduces the compressive stiffness and the residual monomer. The increase in polymerization temperature is associated with the reduction in residual monomer. The residual monomer has an adverse effect on the mechanical properties. The additive percentage and its correlation with both residual monomer percentage and polymerization temperature should be considered to design PMMA combinations that are suitable for a specific mechanical loading conditions.

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