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# Exothermal Characteristics and Release of Residual Monomers from Fiber-reinforced Oligomer-modified Acrylic Bone Cement

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**ABSTRACT:** The aim of this study is to determine the peak temperature of polymerization, the setting time and the release of residual monomers of a modified acrylic bone cement. Palacos<sup>®</sup> R, a commercial bone cement, is used as the main component. The cement is modified by adding short glass fibers and resorbable oligomer fillers, and an additional cross-linking monomer. The test specimens are classified according to the composition of the bone cement matrix (i.e., oligomer-filler, glass-fiber reinforcement, and/or cross-linking monomer). The exothermal characteristics during autopolymerization are analyzed using a transducer connected with a computer. The quantities of residual monomers were analyzed from different test groups using high performance liquid chromatography (HPLC). The  $\Delta T$  value for the oligomer filler and the glass-fiber-containing acrylic bone cement is lower than that for the unmodified bone cement ( $2.1 \pm 0.8^\circ\text{C}$  vs.  $23.5 \pm 4.2^\circ\text{C}$ ). The addition of a cross-linking monomer, EGDMA, shortens the setting time of the autopolymerization of the unmodified bone cement ( $7.1 \pm 0.9$  min vs.  $3.3 \pm 0.3$  min).

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The quantity of the residual monomers released is higher in the modified bone cement than that in the unmodified cement. The cement that contains glass fibers and oligomer fillers has a considerably lower exothermal peak, whereas the total quantity of residual monomers released is increased.

**KEY WORDS:** acrylic bone cement, exothermic characteristics, release of residual monomer.

## INTRODUCTION

**A**crrylic bone cements have been commonly used in orthopedic applications for decades [1]. Their function is to anchor the prosthesis into the bone. The acrylic bone cement is prepared from poly(methylmethacrylate) (PMMA) or related acrylic polymer powders and a monomer liquid that is normally methylmethacrylate (MMA), or MMA mixed with *n*-butyl methacrylate (BMA). There are some disadvantages in the use of orthopedic acrylic bone cements. Among them are the exothermal characteristics of acrylic bone cement during polymerization and the release of the monomer from the uncured cement that can lead to bone tissue necrosis [2–6]. Small amounts of unpolymerized monomers, residual monomers, leach out from the polymerized cement. There are many reports on the determination of the residual monomer in a PMMA matrix [7–14].

The autopolymerization of the acrylic bone cement consists of the free radical polymerization of acrylic monomers. The reaction is initiated by the decomposition of benzoyl peroxide (BPO) that is activated by the presence of a tertiary amine (e.g., *N,N*-dimethyl-*p*-toluidine, DMPT). The autopolymerization of the acrylic bone cement is exothermal, which can give a local temperature peak ranging from 50 to 120°C, depending on the monomer–polymer powder ratio, the composition of the liquid and the solid components, and the quantity of polymerizable cement. There are many reports concerning the exothermal polymerization of acrylic polymers [12,15,16]. After the polymerization, the mixture becomes solid, normally after 10–15 min [15]. The setting time is the polymerization time from mixing to the peak temperature. According to ISO 5833 standard, the setting temperature is defined by the following equation:  $(T_{\max} + T_{\text{ambient}})/2$  [17].

Our previous studies have dealt with the oligomer and the glass-fiber-modified acrylic bone cement composites in a wet environment that led to a porous structure of the acrylic bone cement. Furthermore, the results of our studies have shown that the reduced mechanical properties of the modified bone cement can be offset to some extent by using fiber reinforcement and a semi-interpenetrating network (semi-IPN)

[18–20]. The aim of the present work is to determine the exothermal peak, the setting time, and the amount of leachable residual monomers for modified bone cement.

## MATERIALS AND METHODS

### Materials

The materials used in the study are listed in Table 1. Commercially available Palacos<sup>®</sup> R was used as the bone cement matrix. Table 2 shows the chemical composition of Palacos<sup>®</sup> R as reported by the

*Table 1. The materials used in the study.*

Brand	Manufacturer	Lot No.	Type of Material
EGDMA	Fluka Chemie GmbH, Buchs, Switzerland	421734/1 40302	Cross-linking monomer
Oligomer filler	Biomaterial Research, University of Turku, Turku, Finland	B500mp1	Oligomer
Palacos <sup>®</sup> R powder	Schering-Plough, Labo N.V. Heist-op-den-Berg, Belgium	9-BHAA-2/9068	Polymer
Palacos <sup>®</sup> liquid	Schering-Plough, Labo N.V. Heist-op-den-Berg, Belgium	8-RDCA-41/3002	Monomer
Fiber reinforcement (FR)	Stick Tech Ltd., Turku, Finland	1010321-R-0058	Fibers

*Table 2. Chemical composition of the commercial bone cement (Palacos<sup>®</sup> R) as reported by the manufacturer.*

Powder	40 g
Methyl methacrylate–methylacrylate copolymer	33.8 g
Benzoyl peroxide	0.2 g
Zirconium dioxide	6.0 g
Chlorophyll	0.001 g
Liquid	18.8 g
Methylmethacrylate (MMA) (stabilized with ca 60 ppm hydroquinone)	18.4 g
<i>N,N</i> -Dimethyl- <i>p</i> -toluidine	0.4 g
Chlorophyll-Cu-complex	0.0004 g

manufacturer. An additional cross-linking monomer, ethylene glycol dimethacrylate (EGDMA), was used as a comonomer for MMA. EGDMA (Fluka Chemie GmbH, Buchs, Switzerland) was reagent grade (pure  $\geq 97\%$  using GC) and was used as-received, without removing the inhibitor (i.e., hydroquinone monomethyl ether, ca. 100 ppm). The experimental oligomer that was used as the filler (porogen) was based on an amino acid of trans-4-hydroxy-L-proline that can be polymerized to the corresponding polyester or polyamide [21]. The polyamide of trans-4-hydroxy-L-proline is a brittle and hydrophilic oligomer. The molecular weight of the oligomer varied, but the mean weight was ca. 5000. The brittle oligomer was crushed by hand in a mortar. The particles of the oligomer filler were examined using SEM analysis. The particle size of the oligomer filler varied between 10 and 500  $\mu\text{m}$ . Commercial E-glass fiber reinforcements (FR) for acrylic polymers (Stick Tech Ltd, Turku, Finland) were used. The FR consisted of continuous unidirectional silanized glass fibers that had been preimpregnated with porous PMMA ( $M_w$  220,000) [22]. Before the glass fibers were used for specimen preparation, they were chopped to a length of 2–3 mm.

### Manufacturing of Acrylic Bone Cement Composites

The test specimens were divided into eight groups based on their composition. The composition of each test group ( $N=8$ ) is shown in Table 3. The test specimens were prepared as follows: In Groups 1, 3, 5, and 7, the powder component (i.e., PMMA–PMA copolymer with or without oligomer filler) was mixed with the monomer solution at room temperature (i.e., either (a) MMA in Groups 1 and 3 or (b) a mixture

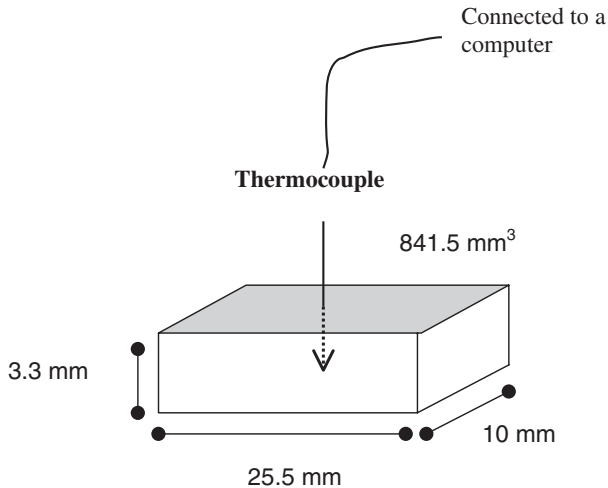
Table 3. The classification of bone cement composites according to concentrations of fillers.

Group	Palacos R /wt%		Cross-linking Monomer /wt%	Oligomer Filler /wt%	Chopped Fibers /wt%
	PMMA–PMA Copolymer /wt%	MMA–Monomer /wt%			
1	68	32	–	–	–
2	60	32	–	–	8
3	48	32	–	20	–
4	40	32	–	20	8
5	68	25.6	6.4	–	–
6	60	25.6	6.4	–	8
7	48	25.6	6.4	20	–
8	40	25.6	6.4	20	8

of MMA and EGDMA in Groups 5 and 7). In Groups 2, 4, 6, and 8, the powder component was mixed with the monomer solution at room temperature, after which E-glass fibers were added. The components were mixed in air in an open bowl by hand. The following observation for specimen manufacture should also be added: when test specimens contained oligomer filler and/or fibers, the equivalent weight of bone cement powder (i.e., PMMA–PMA copolymer) was removed. Similarly, when the cross-linking monomer was added, the same weight of MMA monomer was removed, thus the powder to liquid ratio remained constant.

### Analysis of Exotherm of Autopolymerization

The total quantity of bone cement or modified bone cement for one analysis of polymerization exotherm determination was 2 g. Three parallel polymerization exotherm determinations were done per test group. After mixing the components for 2 min, the dough was packed into a silicon mold ( $3.3 \times 10 \times 25.5 \text{ mm}^3$ ). The cement was polymerized at ambient temperature ( $23^\circ\text{C}$ ). The variation with time of the temperature of the reacting composite mass was registered automatically using a PT-100 transducer connected to a data acquisition collection system (DAQPad-1200, National Instruments Corporation,



**Figure 1.** Schematic diagram of specimens used in determining peak temperature on autopolymerization.

Austin, Texas, USA) that was further connected to a computer. The measuring accuracy of the used system was  $\pm 0.35^\circ\text{C}$ . The transducer was positioned in the center of the uncured cement at a depth of 1.5 mm (Figure 1). The temperature of the composite was registered at 0.25-s intervals for 22 min. The  $\Delta T$  value was calculated using the equation: peak temperature – ambient temperature ( $23^\circ\text{C}$ ). The peak temperature is the maximum temperature attained during the polymerization reaction.

### **Analysis of Released Monomer Content**

The total quantity of bone cement used for analyzing the content of the residual monomers released was 2 g. The mixed dough of bone cement was packed into a silicon mould ( $3.3 \times 10 \times 25.5 \text{ mm}^3$ ) and the cement was allowed to polymerize for 20 min. Three parallel analyses of released monomer contents were done per test group. Therefore, the polymerized cement specimen was cut into small pieces that were divided in three subgroups ( $N=3$ , the weight of each subgroup was between 200 and 350 mg). Each subgroup was incubated in contact with 10 mL of deionized Milli-Q water (electrical resistivity  $18.2 \text{ M}\Omega \text{ cm}$ ) at  $37^\circ\text{C}$  for three days in separate closed plastic Falcon flasks. All the subgroups were separately collected and the supernatants were analyzed using HPLC.

Shimadzu's (LC-2010) modular high performance liquid chromatograph (HPLC) system (Shimadzu Corporation, Kyoto, Japan) was used using the following components (connected with a computer): a system controller (SCL-10Avp), a liquid chromatograph pump (LC-10Advp), a UV-VIS detector (SPD-10Avp), an online degasser (DGU-14A), and an autoinjector (SIL-10Advp). The incorporated columns used in the system were Phenomenex's C18 precolumn (Phenomenex, Torrance, CA, USA) and Phenomenex's C18 analysis column (type: RP18, length: 150 mm, internal diameter: 2 mm, and particle size:  $5 \mu\text{m}$ ). Finally, the collected data were processed using Shimadzu's CLASS VP software.

A sample ( $5 \mu\text{L}$ ) of extraction solution of each subgroup was injected into the chromatograph. The mobile phase used contained methanol, HPLC grade (Rathburn Chemicals Ltd., Walkerburn, Scotland, UK), and Milli-Q water. The analysis was carried out using an isocratic run, where the concentration of methanol was 70 vol.% and the concentration of Milli-Q water ( $18 \text{ M}\Omega \text{ cm}$ ) was 30 vol.% during the run time. The used flow rate was  $0.3 \text{ mL/min}$ , the run time was 15 min, and the used wavelength ( $\lambda$ ) of UV light was 205 nm.

To determine the unknown monomer concentration of cements, a simple calibration curve ( $R^2 > 0.95$ ) was used to predict quantities of the monomers. The calibration was based on five samples with known concentrations of MMA or EGDMA monomers. In the sample solutions, the concentration of residual monomers ( $c_{\text{monomer}}$  ( $\mu\text{g}/\text{mL}$ ),  $c_{\text{MMA}}$ , or  $c_{\text{EGDMA}}$ ) was calculated from the areas under the curve. The amounts of MMA and EGDMA were calculated in ppm.

The following equation was used to calculate the total amount of MMA or EGDMA monomers in the sample solutions,  $m_{\text{monomer}}$  ( $\mu\text{g}$ ) = ( $m_{\text{MMA}}$  or  $m_{\text{EGDMA}}$ ).

$$m_{\text{monomer}}(\mu\text{g}) = [c_{\text{monomer}}(\mu\text{g}/\text{mL}) \times 10 \text{ mL}]$$

This value was used to calculate the weight percentage of the residual monomer (MMA or EGDMA) using the following equation:

$$\text{Residual monomer}(\text{ppm}) = \frac{m_{\text{monomer}}(\mu\text{g}) \times 10^6}{\text{mass of specimen}(\mu\text{g})}$$

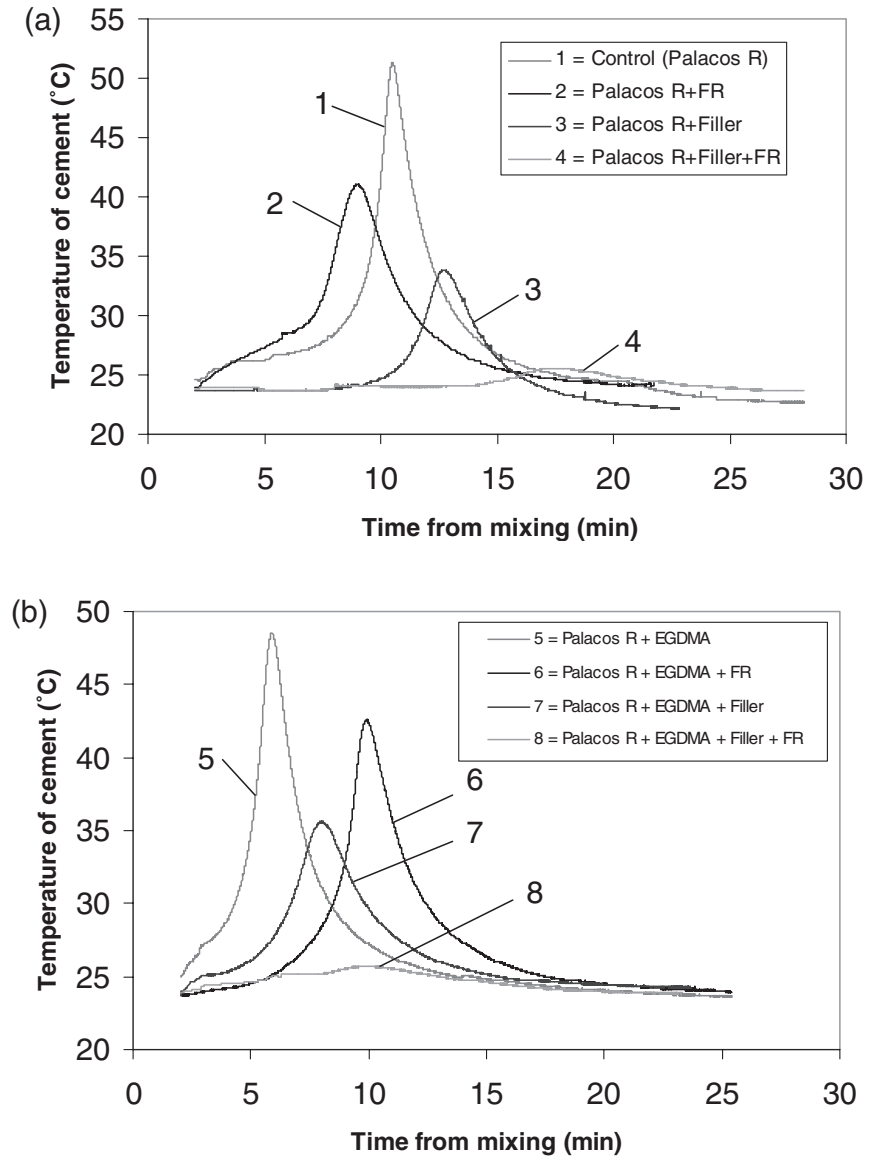
## Statistical Analysis

The statistical analysis was performed using SPSS (Statistical Package for Social Science, SPSS Inc., Chicago, USA) software for Windows with univariate ANOVA, followed by Tukey's post hoc analysis. The fixed factor was the type of the test specimen (i.e., the groups) and the dependent variables were the peak temperature and the quantity of the residual monomer released.

## RESULTS

ANOVA showed that the fixed factor (i.e., the type of the test specimens) had significant effect both on the peak temperature and the quantity of the residual monomer released ( $p < 0.001$ ). Typical exothermal characteristics during the autopolymerization of the bone cement are shown in Figure 2(a) and (b). The peak temperature and the  $\Delta T$  values of cements decreased in the following order: Groups 4 and 8 > Groups 3 and 7 > Groups 2 and 6 > Groups 1 and 5 (Table 4). The peak temperature was attained between 7 and 16 min after mixing the components, when the cements contained only MMA monomer. The setting time was shorter when the cement contained MMA and EGDMA monomers, and the peak temperature obtained was then between 3 and





**Figure 2.** Typical temperature–time graphs: (a) for Group 1 (Control (Palacos R)), Group 2 (Palacos R + FR), Group 3 (Palacos R + Filler), and Group 4 (Palacos R + FR + Filler); and (b) for Group 5 (Palacos R + EGDMA), Group 6 (Palacos R + EGDMA + FR), Group 7 (Palacos R + EGDMA + Filler), and Groups 8 (Palacos R + EGDMA + Filler + FR).

Table 4. The peak temperatures,  $\Delta T$  values, setting temperatures, and setting times of different modifications of bone cement during polymerization.

Group	Peak Temperature /°C	Setting Temperature /°C	$\Delta T$ values /°C	Setting Time /min
1	46.5 ± 4.2	34.7 ± 2.1	23.5 ± 4.2	7.1 ± 0.9
2	37.9 ± 3.0	30.4 ± 1.5	14.9 ± 3.0	5.5 ± 0.3
3	32.0 ± 1.6	27.5 ± 0.8	9.0 ± 1.6	9.7 ± 1.1
4	25.1 ± 0.8	24.1 ± 0.4	2.1 ± 0.8	12.0 ± 0.7
5	48.1 ± 0.7	35.5 ± 0.3	25.1 ± 0.7	3.3 ± 0.3
6	39.6 ± 5.8	31.3 ± 2.9	16.6 ± 5.8	7.1 ± 0.2
7	32.0 ± 3.2	27.5 ± 1.6	9.0 ± 3.2	4.4 ± 0.8
8	25.0 ± 1.0	24.0 ± 0.5	2.0 ± 1.0	6.3 ± 0.2

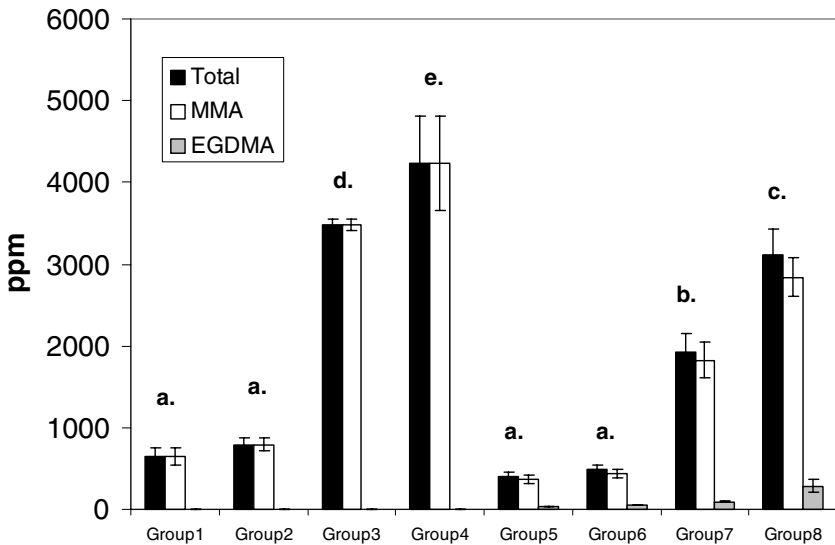


Figure 3. The quantity of released residual monomers according to specimen weight: the quantity of released MMA from Groups 1–4 (i.e., Control (Palacos R), Palacos R + FR, Palacos R + Filler, and Palacos R + FR + Filler); the quantity of released total monomer from Groups 5–8 (i.e., Control (Palacos R), Palacos R + EGDMA, Palacos R + EGDMA + FR, Palacos R + EGDMA + Filler, and Palacos R + EGDMA + Filler + FR). The same superscript letter indicates no significant statistical difference.

8 min. Figure 3 shows the results for the released monomers of MMA and EGDMA. According to these results, the highest quantities of residual monomers were leached into water from the cement that contained glass fibers and the oligomer filler. The quantity of the residual monomer varied between 366 and 4200 ppm.

## DISCUSSION

In this study, the modified bone cements consisted of two components: fillers (i.e., hydrophilic oligomer and/or glass fibers) in PMMA–PMA powder, and the liquid (i.e., MMA or a mixture of MMA–EGDMA). The unmodified Palacos<sup>®</sup> R served as the control group (Group 1). Seven modifications of bone cements were prepared by changing the composition of powder components and/or the liquid component by replacing 6.4 wt% of MMA and replacing it with a cross-linking monomer (EGDMA). The polymerization of MMA, in the presence of EGDMA and PMMA, leads to the formation of a three-dimensional network (i.e., semi-IPN structure) [23–25].

In Figure 2(a) and (b), the typical exothermal characteristics of each modification are shown: (a) peak temperature and (b) setting time. It was noticed that the addition of a cross-linking monomer to the bone cement matrix did not significantly change the peak temperature. However, the setting time was slightly shortened by the presence of EGDMA, probably because the bifunctional methacrylate (EGDMA) increased the velocity of polymerization by providing more reactive groups for free radical polymerization. Moreover, it was noticed that the addition of fibers did not significantly increase the amount of residual monomers. However, the presence of fibers slightly reduced the peak temperature. Using glass fibers and the oligomer filler, the increased velocity of polymerization, affected by EGDMA, was eliminated.

Heat formation during the polymerization reaction of acrylic bone cement can lead to the necrosis of bone. One aspect of this research was to evaluate whether the modified bone cement that has been the subject of an earlier study [19,20] could have improved exothermal characteristics over that of the unmodified acrylic bone cement. According to the results of this study, the peak temperature of cement decreased considerably when the cement contained fillers and fibers in the matrix. It should be noted that when fillers were added to the cement system, the weight fraction of the polymerized monomer system was kept the same. From a methodological point of view, it is possible that the hand-mixed cements had led to the concentration of fillers near the transducer, and this could have led to somewhat lower local  $\Delta T$  values, which actually occurred in the bulk cement. To overcome this possible problem, a calorimetric analysis of the exothermal characteristics needs to be done.

In this study, Groups 4 and 8 had much lower peak temperatures than the bone cement without fillers and glass fibers. This suggests that the presence of fillers might disturb the free radical polymerization. The

following mechanisms are possible: (a) the concentration of initiator in the monomer system of the cement was not optimal; (b) the concentration of accelerator was not optimal; (c) the fillers might have contained air and thus O<sub>2</sub> inhibition of the free radical polymerization has occurred; and (d) the fillers were not homogeneously distributed in the bone cement. Moreover, when the test specimens contained oligomer filler and/or fibers, the equivalent weight of PMMA–PMA copolymer was removed. Therefore, the addition of the oligomer filler and fibers changed the PMMA–PMA copolymer–MMA monomer ratio of the conventional bone cement and the viscosity of the mixture, which decreases further the mobility of the reaction monomers and then prevents the autoacceleration. Also, the solubility of PMMA–PMA copolymer or its modified counterpart in MMA might be different compared to their solubility in EGDMA, which can also affect the viscosity of the mixture. Therefore, the rheology of the modified bone cement needs to be studied more thoroughly in the near future.

HPLC was used for the determination of the released MMA and EGDMA in water without the need for a preliminary extraction from the media, because both the monomers are soluble in aqueous solvents. The information about the extracted residual monomer content of these bone cement composites was analyzed from deionized water after 3 days' incubation at 37°C, and the quantifying of these media. It has been shown that the majority of the residual monomers of the PMMA-based materials are released during the first two days, and that the amount of released residual monomers correlates with the reduction in residual monomer content of the polymer [7]. On the basis of this, the three days' water immersion time was selected for this study. An increased residual monomer content was noticed when the composite contained fillers (Groups 3, 4, 7, and 8). This could be due to the lower exothermal temperature of the cement that contained fillers and fibers. It has been shown that thick resin specimens made by the PMMA–MMA system, which have a higher exothermal peak, produce PMMA that contains less residual monomers than thinner specimens [16,26]. In addition, the hydrophilicity of the oligomer filler may result in poor wetting by the monomer and thus poorer contact at the interface. This may also affect elution of residual monomer as the materials containing the oligomer may absorb more water. Generally, the level of MMA released from bone cement was lower compared to those values found with similar autopolymerized denture-base polymers. This might be due to the variations in the initiator–activator systems or in the used powder/liquid ratio. Moreover, when glass fibers were added to the powder-liquid type acrylic resin system, the quantity of the released residual

MMA was shown to increase [27], a finding, which was also confirmed by the present study.

The addition of a cross-linking monomer of EGDMA reduced the quantity of released monomers. This suggests that the presence of a bifunctional monomer can improve the polymerization process of the monomer system based mainly on monofunctional monomers. Because of the possibility of bifunctional monomers forming pendant molecules in PMMA backbones, instead of remaining as actual residual monomers in the polymers, more detailed information on the polymerization needs to be obtained by measuring the degree of conversion (DC%) of the functional groups. The FTIR method could be used for DC% determination.

## CONCLUSIONS

Within the limitations of the study, the following conclusions were drawn: (1) By adding glass fibers and oligomer fillers to the bone cement, the exothermal peak was lowered considerably. (2) By adding oligomer fillers to the bone cement, the total quantity of released residual monomers was increased. (3) By adding a cross-linking monomer to the bone cement, the residual monomer release was lower compared to the control cements.

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