ASEC 2022

MDPI

Proceeding Paper

Curing Characteristics of Urethane-Dimethacrylate Homopolymers and Their Composites for Potential Application in Bone Cement †

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† Presented at the 3rd International Electronic Conference on Applied Sciences; Available online: https://asec2022.sciforum.net/.

Abstract: The polymerization of methacrylate compositions used in bone cement is often accompanied by a strong exothermic effect. The polymerizing mass heats up to very high temperatures at the cement application site, irritating the adjacent tissues and even cell death. On the other hand, a bone cement composition should have optimal curing time, which should be long enough to allow for proper preparation of the cement and short enough to prevent leaking of the cement out of the restoration place. Therefore, new compositions are sought to reduce the curing temperature of bone cement and maintain a sufficiently long curing time. Our proposal is based on using five homopolymers obtained by polymerizing urethane-dimethacrylates. They were composed of diisocyanate cores: tolylene 2,4 diisocyanate (TDI), isophorone diisocyanate (IPDI), 4,4′-methylenebis(cyclohexyl isocyanate) (CHMDI), and di-, tri-, and tetraethylene glycol monomethacrylate wings (respectively DEGMMA, TEGMMA, TTEGMMA). The following monomers were obtained: DEGMMA/CHMDI, TEGMMA/IPDI, TEGMMA/TDI, TEGMMA/CHMDI, and TTEGMMA/CHMDI. Neat homopolymers as well as their composites with barium sulfate and hydroxyapatite were tested for curing temperature and time. Almost all proposed systems were characterized by appropriate values of both parameters. The presence of fillers positively affected the studied parameters by lowering the polymerization temperature and time.

Keywords: bone cement; urethane-dimethacrylates; homopolymers; composites; polymerization parameters

Citation: Chrószcz-Porębska, M.W.; Barszczewska-Rybarek, I.M. Curing Characteristics of Urethane-Dimethacrylate Homopolymers and Their Composites for Potential Application in Bone Cement. **2022**, *4*, x. https://doi.org/10.3390/xxxxx

Academic Editor(s):

Published: 1 December 2022

1. Introduction

The development of poly(methyl methacrylate) (PMMA) based bone cements (PMMA-BCs) by Charnley in 1958 revolutionized the orthopedic surgical technologies [1]. Since then, they are widely used to stabilize hip and knee implants as well as bone fillers [2]. They consist of two phases: solid and liquid. A solid phase contains powdered PMMA, polymerization initiator, inorganic fillers, and sometimes antibacterial additives such as antibiotics. A liquid phase consists of methyl methacrylate (MMA), polymerization accelerator, and stabilizer [1]. The frequency of PMMA-BCs application arises from their functional properties (good mechanical and physicochemical properties, high injection ability), ease of handling, good primary fixation between bone and cement, and economic reasons [3,4]. However, the main concern is that the polymerization of MMA is a strongly

exothermic process, resulting in an increase in the temperature of tissue adjacent to the application site of PMMA-BCs. The highest curing temperature (T_c) recorded for the PMMA-BCs was 120 °C [5]. This value significantly exceeded the value of 90 °C, which is the maximum T_c specified for this type of material [6]. It is also worth mentioning that such high polymerization temperatures can cause the necrosis of bone tissue (the temperature at which the necrosis of bone tissue begins is 50 °C) [7]. Bone cements should also have optimal curing time (t_c). It should be long enough to ensure proper preparation of the material and short enough to prevent its leaking out of the restoration place. According to ISO 5833:2002 standard, the t_c from 3 to 5 min is recommended for PMMA-BCs [6]. Therefore, the development of new compositions characterized by low T_c and suitable t_c is one of the current trends in designing bone cements based on methacrylates.

The novel generation of bone cements is based on dimethacrylates. The first commercially available bone cement based on dimethacrylates was Cortoss ® (Styker, USA). It consisted of bisphenol A glycerolate dimethacrylate (Bis-GMA), ethoxylated Bis-GMA derivative (Bis-EMA), and triethylene glycol dimethacrylate (TEGDMA). Compared to the PMMA-BCs, it has lower T_c and more suitable mechanical and physicochemical performance. However, it contains the bisphenol A moieties that can release from the material to the human organism and thus disrupt hormonal balance and negatively affect the immune, reproductive, and neuroendocrine systems [8].

Our proposal is based on using homopolymers obtained by polymerization of urethane-dimethacrylate derivatives (UDMAs) as alternatives for the currently used dimethacrylates. They are composed of diisocyanate cores: tolylene 2,4 diisocyanate (TDI), isophorone diisocyanate (IPDI), 4,4′-methylenebis(cyclohexyl isocyanate) (CHMDI), and di-, tri-, and tetraethylene glycol monomethacrylate wings (respectively DEGMMA, TEGMMA, TTEGMMA). They are abbreviated as DEGMMA/CHMDI, TEGMMA/CHMDI, TTEGMMA/CHMDI, TEGMMA/IPDI, and TEGMMA/TDI (Figure 1).

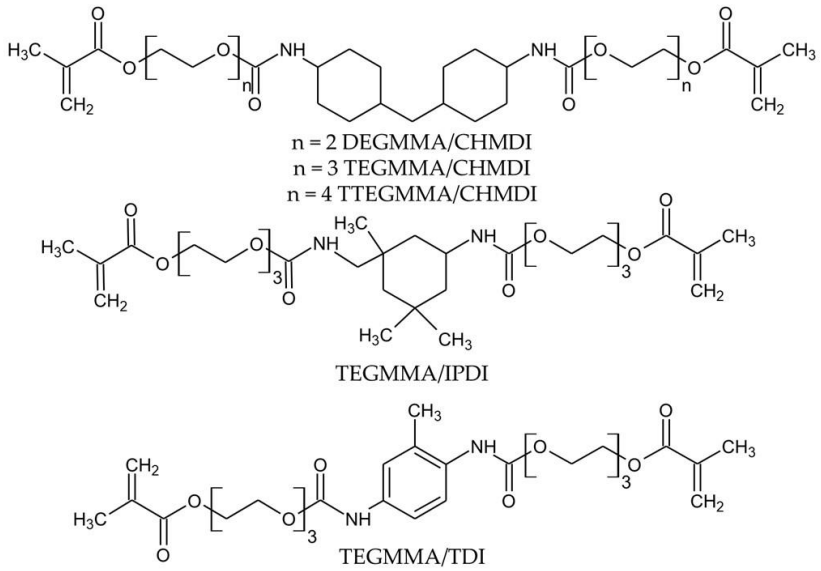


Figure 1. Chemical structure of dimethacrylate monomers used in this study.

Monomers used in this study were selected from the group of 24 urethane-dimethacrylates described in the literature [9]. The selection was made on the basis of the properties of monomers and their corresponding polymers: (i) liquid state of monomers, (ii) low monomer viscosity, suitable for application with the use of a syringe, (iii) polymer glass transition temperature higher than 40 °C, (iv) polymer modulus lower than 3000 MPa, (v) degree of double bond conversion in polymer higher than 50 %, and (vi) polymer water sorption lower than 40 μg/mm^3.

Monomers and their compositions with 10 wt.% hydroxyapatite and 20 wt.% barium sulfate were cured via low-temperature polymerization. Obtained cured materials were tested for curing temperature and time.

2. Materials and Methods

2.1. Chemicals and Reagents

Urethane-dimethacrylate derivatives: DEGMMA/CHMDI, TEGMMA/CHMDI, TTEGMMA/CHMDI, TEGMMA/IPDI, and TEGMMA/TDI were obtained from oligoethylene glycol dimethacrylates (OEGMMA) and diisocyanates according to the procedure described in [10]. OEGMMAs: DEGMMA, TEGMMA, and TTEGMMA were synthesized by transesterification of MMA (methyl methacrylate, Acros Organics, Geel, Belgium) with respectively: DEG (diethylene glycol), TEG (triethylene glycol), and TTEG (tetraethylene glycol) (all purchased from Acros Organics, Geel, Belgium) according to the procedure described in [10]. $BaSO_4$ (barium sulfate), BPO (benzoyl peroxide), DMPT (N,N-dimethyl-p-toluidine), HA (hydroxyapatite), PTZ (phenothiazine), and diisocyanates: CHMDI (4,4′-methylenebis(cyclohexyl isocyanate), IPDI (isophorne diisocyanate), TDI (tolylene 2,4 diisocyanate) were purchased from Sigma-Aldrich (St. Louise, MO, USA) and used as received.

2.2. Curing Procedure

Homopolymers were obtained through low-temperature polymerization. Polymerization was performed in a glass test tube with the use of BPO (polymerization initiator) and DMPT (polymerization accelerator) in a weight ratio specified for each monomer (Table 1). Composites were obtained by polymerization of a homogeneous mixture of monomers with 20 wt.% $BaSO_4$ and 10 wt.% HA, with the use of the BPO/DMPT ratios the same as for the neat homopolymers.

Table 1. Weight ratios of BPO and DMPT used for the low-temperature polymerization.

Monomer	BPO (wt.%)	DMPT (wt.%)
DEGMMA/CHMDI	0.5	0.15
TEGMMA/CHMDI	0.6	0.15
TTEGMMA/CHMDI	0.6	0.15
TEGMMA/IPDI	1.1	0.2
TEGMMA/TDI	0.4	0.15

2.3. Curing Temperature and Time

Curing temperature (T_c) and time (t_c) were determined utilizing a waterproof, highly accurate thermometer Elmetron PT-400 (Elmetron, Zabrze, Poland). The temperature during curing was checked every 10 s. The measurement started soon after the introduction of DMPT into the monomer system containing BPO and inorganic fillers (in case of composites).

T_c was calculated according to the equation:

$$T_c(℃) = \frac{T_0 - T_{max}}{2}, \quad (1)$$

where: T_0—initial temperature of monomer composition (°C), T_{max}—maximum curing temperature (°C). t_c was taken from the graph $T = f(t)$ for T_c.

The relationship between the polymerization time (t) and temperature (T) for neat homopolymers and their corresponding composites are shown in Figure 2.

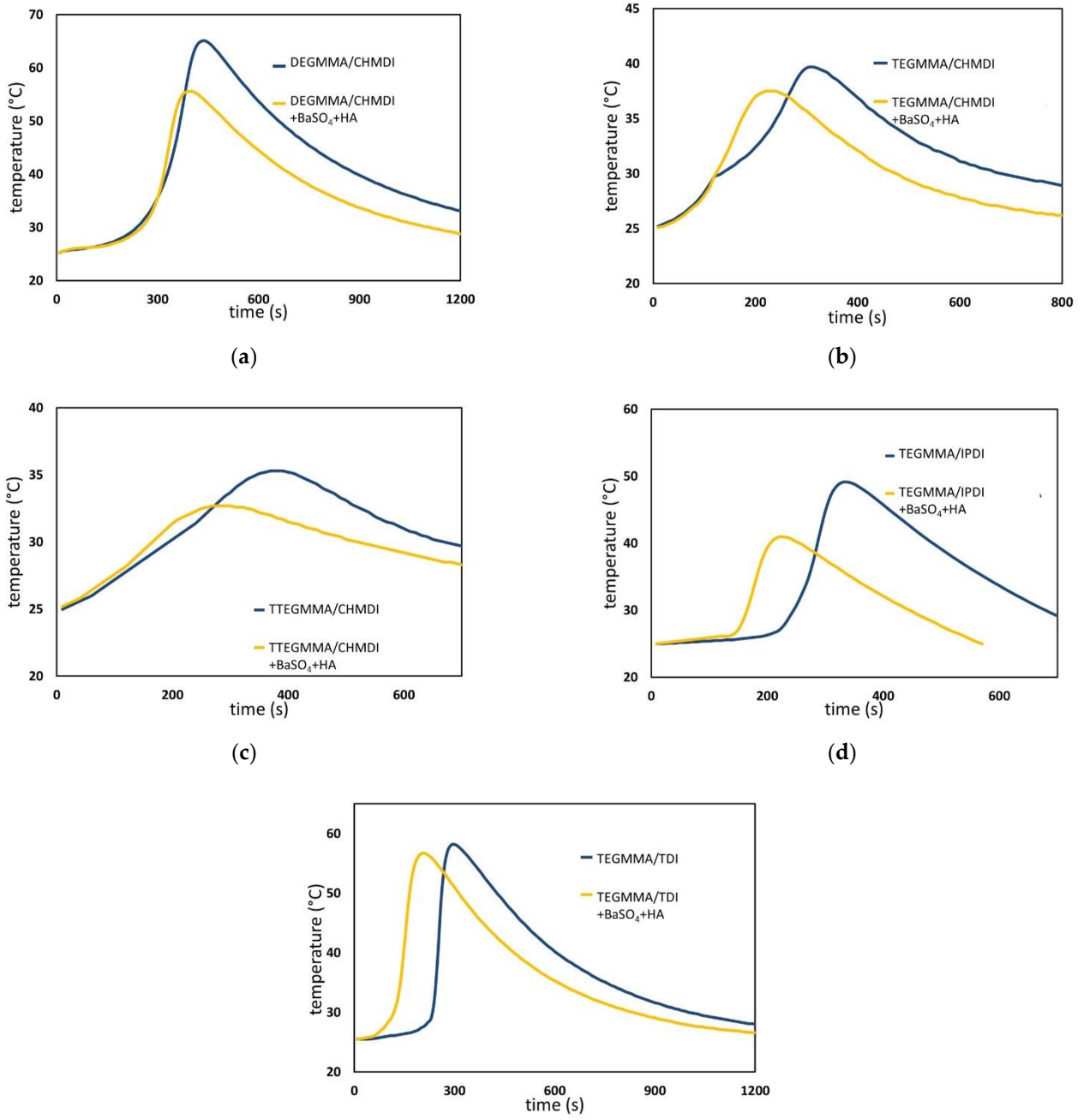


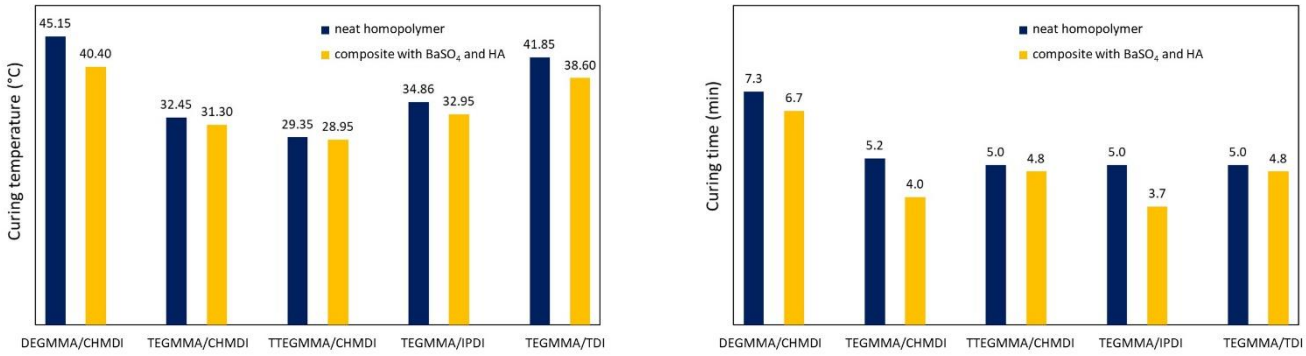
Figure 2. Relationship between polymerization time and temperature for (**a**) DEGMMA/CHMDI; (**b**) TEGMMA/CHMDI; (**c**) TTEGMMA/CHMDI; (**d**) TEGMMA/IPDI; (**e**) TEGMMA/TDI and their composites with $BaSO_4$ and HA.

3. Results

In this work, five UDMAs synthesized according to the procedure described in [10], and their compositions with 20 wt.% $BaSO_4$, and 10 wt.% HA were subjected to low-temperature polymerization. Neat homopolymers and composites were tested for their T_c and t_c. Obtained results are shown in respectively Figure 3a,b.

The T_c of neat homopolymers ranged from 29.35 to 45.15 °C. The highest T_c was recorded for the DEGMMA/CHMDI, whereas the lowest T_c was recorded for the TTEGMMA/CHMDI. Within the neat homopolymers with the CHMDI core, the T_c decreased with the lengthening of the oligooxyethylene chains. The T_c of composites ranged

from 28.95 to 41.85 °C and was lower than the T_c of corresponding neat homopolymers. The highest T_c was recorded for the DEGMMA/CHMDI-based composite, whereas the lowest T_c was recorded for the TTEGMMA/CHMDI-based composite.



(**a**) (**b**)

Figure 3. The (**a**) curing temperature and (**b**) curing time of studied neat homopolymers and their corresponding composites with $BaSO_4$ and HA.

The t_c of neat homopolymers ranged from 5.0 to 7.3 min. The highest t_c was recorded for the DEGMMA/CHMDI, whereas the lowest t_c was recorded for three homopolymers: TTEGMMA/CHMDI, TEGMMA/IPDI, and TEGMMA/TDI. Within the homopolymers with the CHMDI core, the t_c decreased with the lengthening of the oligooxyethylene chains. The t_c of composites ranged from 3.7 to 6.7 min and was lower than the t_c of corresponding neat homopolymers. The highest t_c was recorded for the DEGMMA/CHMDI-based composite, whereas the lowest t_c was recorded for the TEGMMA/IPDI-based composite.

4. Discussion

The main concern about the application of PMMA-BCs is their high polymerization temperature. Therefore, they can irritate adjacent tissues or even cause cell necrosis. For this reason, alternative methacrylate monomers are being sought, which can offer a bone cements of low polymerization temperature.

In this study, five UDMA homopolymers and their composites with 20 wt.% $BaSO_4$, and 10 wt.% HA were checked for their polymerization temperature and time to verify the possibility of using them as bone cements. Homopolymers and their corresponding composites were obtained by low-temperature polymerization utilizing the BPO/DMPT initiating system.

All UDMA monomers were characterized by T_c lower than 90 °C, which means that they fulfilled the requirements for bone cements, according to ISO 5833:2002 standard [6]. The DEGMMA/CHMDI neat homopolymer showed the highest T_c of 45.15 °C. It implies that the polymerization of tested UDMAs will not cause morphological bone tissue damage and cell necrosis, which occur at respectively 47 and 50 °C [11]. The enrichment of UDMAs with inorganic fillers in each case caused a decrease in T_c value. The greatest difference of 10.52 % was observed for the DEGMMA/CHMDI, whereas the lowest difference of 1.36 % was observed for the TTEGMMA/CHMDI. The highest T_c observed for studied composites was slightly higher than the temperature inside the human body, which suggests that their polymerization would not have any adverse effect on adjacent tissues.

According to ISO 5833:2002 standard [6], bone cement should have a t_c within the range of 3 to 5 min. Almost all of tested UDMAs met this requirement. TTEGMMA/CHMDI, TEGMMA/IPDI, and TEGMMA/TDI fall within the upper limit of the recommended scope, as they were characterized by a t_c of 5 min. DEGMMA/CHMDI

and TEGMMA/CHMDI were characterized by longer t_c, however only DEGMMA/CHMDI significantly exceeded the acceptable value. The differences between the t_c and maximum t_c specified for bone cements were respectively 46 and 4 %. Similarly to T_c, the enrichment of UDMAs with inorganic fillers in each case caused a decrease in t_c. The greatest difference of 26.00 % was observed for TEGMMA/IPDI, whereas the lowest difference of 4.00 % was observed for TTEGMMA/CHMDI and TEGMMA/TDI. Concerning the ISO 5833:2002 standard, all composites were characterized by appropriate t_c, except DEGMMA/CHMDI-based composite, which have significantly higher t_c.

5. Conclusions

All proposed UDMA systems were characterized by appropriate values of T_c, which were significantly lower than that specified by ISO standard. Obtained values were also lower than the temperature of cell necrosis implying that their polymerization will not negatively affect the adjacent tissues. Almost all systems were characterized by suitable t_c, except the DEGMMA/CHMDI and TEGMMA/CHMDI, which had t_c longer than 5 min. The presence of inorganic fillers positively affected the studied parameters by lowering the T_c and t_c. After their introduction, only DEGMMA/CHMDI-based composite did not fulfill the requirements for bone cement due to incorrect t_c.

Author Contributions: Conceptualization, I.M.B.-R.; methodology, I.M.B.-R.; investigation, I.M.B.-R. and M.W.C-P.; resources, I.M.B.-R. and M.W.C.-P.; data curation, M.W.C.-P.; writing—original draft preparation, M.W.C.-P. and I.M.B.-R.; writing—review and editing, I.M.B.-R.; visualization, M.W.C.-P.; supervision, I.M.B.-R.; project administration, I.M.B.-R.; funding acquisition, M.W.C.-P. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Rector's grant for the scientific research and development activities in the Silesian University of Technology, grant number: 32/014/RGJ22/2004.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data supporting reported results are available from the authors.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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