Synthesis, characterization and evaluation of urethane derivatives of Bis-GMA

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Abstract

Objectives. The aims of the study were to synthesize derivatives of Bis-GMA having pendant n-alkyl urethane substituents and to characterize and evaluate their physicochemical properties.

Methods. Stoichiometric amounts of Bis-GMA and n-alkyl isocyanates were reacted in dichloromethane with dibutyltin dilaurate as a catalyst. Volumetric shrinkage, water uptake, degree of vinyl conversion, refractive index and viscosity of resulting urethane monomers and those of Bis-GMA were measured. The flexural strengths of their corresponding homopolymers and that of Bis-GMA were also measured.

Results. These types of urethane derivatives of Bis-GMA exhibited lower viscosities and were more hydrophobic than Bis-GMA. Generally, the viscosity of these experimental monomers decreased with increasing chain length of the alkyl urethane substituent. Photopolymerization of the new monomers gave high degrees of vinyl conversion compared to Bis-GMA. The experimental monomers also yielded polymers with lower polymerization shrinkages at equivalent degrees of vinyl conversion, than Bis-GMA. The refractive indices of these urethane derivatives were similar to Bis-GMA, but the flexural strengths of their polymers were lower than that of the Bis-GMA homopolymer, decreasing with increasing chain length of the alkyl urethane substituent.

Significance. Because of their excellent overall properties, these new derivatives of Bis-GMA have potential as dental monomers that can improve many properties of resin based dental materials that utilize methacrylate monomer systems.

Keywords: Bis-GMA; Dimethacrylate; Urethane; Polymerization shrinkage; Conversion; Viscosity; Alkyl isocyanate; Hydrogen bonding

1. Introduction

Bis-GMA, 2,2-bis[p-(2’-hydroxy-3’-methacryloxypropoxy)phenyl]propane, is widely used as a base monomer in polymeric dental materials, e.g. restorative composites, adhesives and prophylactic sealants. This monomer, which also is used as a commercial vinyl ester matrix monomer for structural composites, is synthesized by reacting glycidyl methacrylate with bisphenol A, or alternatively, by reacting the diglycidyl ether of bisphenol A and methacrylic acid [1]. The structure of the major product of these addition reactions, assigned the acronym Bis-GMA, is shown below.

Advantages of using Bis-GMA over smaller-sized dental monomers, such as methyl methacrylate, include lower volatility and diffusivity into tissues and the formation of higher moduli polymers with less volume contraction [2]. These desirable properties of Bis-GMA are partially negated by its relatively high viscosity and low vinyl conversion under ambient polymerization conditions. To overcome these deficiencies, a less viscous monomer is needed as a diluent comonomer; e.g. triethylene glycol dimethacrylate (TEGDMA) is frequently used to achieve a dental resin of workable viscosity.

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Unfortunately, the addition of smaller-sized diluent comonomers such as TEGDMA, while increasing vinyl conversion, also increases polymerization shrinkage and contributes to the development of concomitant stress sites in the polymeric dental composites and at the interfaces with tooth structure, resulting in interfacial gaps that can promote microleakage. However, the relatively high hydrophilicity and penetrability to tissues of TEGDMA raise biocompatibility issues, and recent studies have suggested that TEGDMA should be replaced by larger, more hydrophobic and biocompatible monomers [3]. Moreover, the hydroxyl groups of Bis-GMA are a major source of not only the high viscosity of this monomer but also contribute significantly to the relatively high water absorption of Bis-GMA based polymeric matrices. Excessive water absorption can have adverse effects on the properties of dental composites by plasticization of the matrices by water and also by promoting possible hydrolytic degradative reactions.

The high viscosity of Bis-GMA, derived primarily from the hydrogen bonding of the hydroxyl groups, can be reduced by their conversion to other functional groups such as esters [4]. This can lead to derivative monomers that are less viscous and less hydrophilic than Bis-GMA, but that also yield polymers with lower flexural strength and moduli. Another approach to less viscous and more hydrophobic monomers involves removal of pendant hydroxyl groups by substitution of several backbone ethylene oxide groups between the bisphenol A core and the methacrylate groups; these monomers also yield polymers with relatively lower flexural strengths and moduli compared to Bis-GMA polymers. These and other similar types of derivatives of Bis-GMA [2,4–6], however, should be useful as compatible, low shrinking diluent comonomers for Bis-GMA and similar base dental monomers.

In this study, we have reacted Bis-GMA with monofunctional alkyl isocyanates (RNCO) of varying chain length. The resulting pendent urethane groups are known to form weaker hydrogen bonds compared to the hydroxyl group but are expected to have higher cohesive energy density than ester or ether linkages. These urethane derivatives of Bis-GMA also are expected to have much lower viscosities and water uptake than Bis-GMA, and exhibit higher conversion of vinyl groups without increasing (and perhaps decreasing) polymerization shrinkage of dental resin systems.

2. Materials and methods

2,2-bis[p-(2′-hydroxy-3′-methacryloxypropoxy)phenyl]propane, Bis-GMA and TEGDMA were obtained from Esstech, Essington, PA, USA, and used as received. The n-alkyl isocyanates, dibutyltin dilaurate, dichloromethane, camphorquinone and ethyl-4-N,N-dimethylaminobenzoate were obtained from Aldrich Chemical Company Inc., Milwaukee, WI, USA, and were used as received. Using a previously described procedure [7], Bis-GMA was reacted with stoichiometric amounts of the various alkyl isocyanates (ethyl, n-propyl, n-butyl, n-hexyl and n-octyl isocyanates) in dry dichloromethane under reflux conditions (at approximately 40 °C for 1–2 d) as shown in Fig. 1.

Catalytic amounts (0.01–0.02 mol fraction %) of dibutyltin dilaurate were added to the reaction mixtures, and the reactions were followed by FTIR spectroscopy by monitoring the disappearance of isocyanate absorption band at 2270 cm⁻¹; the urethane-substituted monomers were formed in quantitative yield. After solvent removal by rotary evaporation under increasing vacuum, FTIR and ¹H NMR of the residual liquids were recorded to confirm the structures of the products and also to ensure the complete removal of dichloromethane. Refractive index was measured using a Bausch & Lomb refractometer at 22.5 °C. The relative standard uncertainty for this measurement was 0.5%. Viscosity was measured with a Rheometric Scientific ARES controlled-strain rheometer, in the steady rate sweep mode. Measurements were made in both clockwise and counter-clockwise directions, and then averaged. In each direction, at each shear rate, shear was applied for 100 s before measuring, and then the torque was measured for 30 s. The fixtures used were 25 mm, 0.04 rad cone and plate. All measurements were made at 25 °C. The relative standard uncertainty in each point was 0.5%.

Camphorquinone (mole fraction, 0.6%) and ethyl-4-N,N-dimethylaminobenzoate (mole fraction, 2%) were used as the visible light (470 nm) photoinitiator system. For the determination of degree of vinyl conversion, monomer specimens in Teflon molds (5 mm diameter and 1.5 mm thickness) were irradiated with Spectrum Curing Visible Light (Caulk/Dentsply) for 60 s followed by a postcure period of 60 min and then another irradiation for 30 s.

1 Disclaimer. Certain commercial materials and equipment are identified in this work for adequate definition of the experimental procedures. In no instance does such identification imply recommendation or endorsement by the National Institute of Standards and Technology or that the material and the equipment identified is necessarily the best available for the purpose.
The degree of vinyl conversion was determined by near infrared spectroscopy [8]. The vinyl double bond of these methacrylate monomers appears at 6165 cm$^{-1}$ in the near infrared region. For calculating the degree of vinyl conversion this peak area was compared in the monomer and in the photocured polymer using one specimen for each urethane-modified monomer. The ratio of area normalized to the thickness of the sample leads to the degree of vinyl conversion. The relative standard uncertainty in each point was 0.7%. Volumetric shrinkage was measured using a computerized mercury dilatometer [9,10], which used a Spectrum Curing Visible Light (Caulk/Dentsply). Weighed specimens of each monomer on glass slides were irradiated for 60 s and then, after 60 min, the specimens were subjected to a second irradiation for 30 s.

Flexural strength (FS) was measured in the three point bending mode (Instron 5500R) on five specimens (approximately 27 mm $\times$ 2 mm $\times$ 2 mm) cured for 60 s per side with the TRIAD 2000 photocuring unit (Dentsply). Water uptake was measured by soaking known masses of the vacuum dried photopolymerized polymers (5 mm diameter and 1.5 mm thickness) in distilled water at room temperature and then recording the mass gain of the polymers with time.

### 3. Results and discussion

The dimethacrylates Bis-GMA and 1,6-bis(methacryloxy-2-ethoxycarbonylamino)-2,4,4-trimethylhexane (UDMA) are widely used as the primary or base monomers in the formation of the polymeric matrices of dental composites. These two monomers are comparable in size but differ in their chemical structural features which affect critical properties such as viscosity, diffusivity, polymerization, vinyl conversion, shrinkage, water uptake, optical match with reinforcing fillers, physicochemical and mechanical properties. A common feature of Bis-GMA and UDMA is their ability to form physical crosslinks via hydrogen bonding that can augment the basic strength and modulus of their dimethacrylate-based polymers that is principally achieved by carbon–carbon covalent bonding, especially in the form of chemical crosslinks of the network structure.

This study was designed to ascertain how the conversion of the hydroxyl groups of Bis-GMA to derivatives without hydroxyl groups but with pendent alkyl urethane substituents of varying chain length would affect critical properties of the new monomers, namely, viscosity, vinyl conversion, polymerization, shrinkage, and hydrophobicity. From this study it was clear that both the nature of hydrogen bonding in the monomers (hydroxyl-mediated in Bis-GMA versus urethane mediated in the case of the new monomers) and the length of the alkyl substituents are important parameters to consider in the design of monomers or monomer systems with optimal properties.

The reaction of $n$-alkyl isocyanate with Bis-GMA also can be varied as to stoichiometry to control the properties of the new monomers. The $–$OH group of Bis-GMA has a broad peak in FTIR centered at 3492 cm$^{-1}$, and this peak gradually diminished as the reaction progressed and was replaced by a new peak corresponding to the urethane group centered at 3373 cm$^{-1}$. This reaction also can be extended to other straight chain alkyl isocyanates (RNCO), as well as to branched chain and cyclic isocyanates. The isocyanates employed in this study were used to assess the effect of alkyl chain length of the urethane monomers on their properties and that of their polymers.

An important consideration in the formulation of durable, esthetic dental composites is not only high vinyl conversions with low polymerization shrinkage but also how well the refractive indices of the polymer matrices match those of the reinforcing fillers. Typical radiopaque fillers such as those containing barium, strontium and zirconium have refractive indices of about 1.55. Table 1 includes the refractive index and the degree of vinyl conversion for the urethane modified Bis-GMAs. The refractive indices of these new urethane monomers are comparable to Bis-GMA but decrease somewhat as the length of the alkyl side chain is increased. The refractive index of TEGDMA, a widely used diluent for Bis-GMA, is only 1.460. Hence, its addition to Bis-GMA will not only decrease resin viscosity but also lower the refractive

<table>
<thead>
<tr>
<th>Resin</th>
<th>RI at 22.5 $^\circ$C</th>
<th>Vinyl conversion (%)</th>
<th>Volumetric shrinkage (%)</th>
<th>Shrinkage extrapolated to 100% conversion</th>
<th>Zero shear viscosity (Pa s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bis-GMA</td>
<td>1.549</td>
<td>41.46</td>
<td>3.43 (0.06)</td>
<td>8.26</td>
<td>538.00 (0.60)</td>
</tr>
<tr>
<td>Bis-GMA/EnNCO</td>
<td>1.530</td>
<td>55.22</td>
<td>4.20 (0.01)</td>
<td>7.59</td>
<td>236.19 (1.31)</td>
</tr>
<tr>
<td>Bis-GMA/PnNCO</td>
<td>1.524</td>
<td>63.75</td>
<td>4.15 (0.12)</td>
<td>6.59</td>
<td>61.53 (0.26)</td>
</tr>
<tr>
<td>Bis-GMA/BuNCO</td>
<td>1.518</td>
<td>66.58</td>
<td>4.18 (0.15)</td>
<td>6.28</td>
<td>24.68 (0.19)</td>
</tr>
<tr>
<td>Bis-GMA/HexNCO</td>
<td>1.516</td>
<td>75.12</td>
<td>4.20 (0.01)</td>
<td>5.59</td>
<td>16.87 (0.14)</td>
</tr>
<tr>
<td>Bis-GMA/OctNCO</td>
<td>1.513</td>
<td>73.88</td>
<td>4.08 (0.05)</td>
<td>5.52</td>
<td>36.94 (0.18)</td>
</tr>
<tr>
<td>Bis-GMA/(Bis-GMA/BuNCO) (50:50)</td>
<td>1.531</td>
<td>63.20</td>
<td>3.86 (0.52)</td>
<td>6.13</td>
<td></td>
</tr>
<tr>
<td>Bis-GMA/TEGDMA (50:50)</td>
<td>1.507</td>
<td>67.30</td>
<td>8.31 (0.43)</td>
<td>12.34</td>
<td></td>
</tr>
</tbody>
</table>

The value in parenthesis is the average standard deviation of mean value derived from three measurements.
index of the resin system, thereby reducing its optical match with the usual radiopaque glass filler systems. The widely used alternative monomer to Bis-GMA, UDMA, has a refractive index of 1.480, compared to a refractive index of 1.507 for a 50:50 by mass fraction mixture of Bis-GMA and TEGDMA. By contrast, a 50:50 by mass fraction mixture of Bis-GMA and Bis-GMA/BuNCO has refractive index of 1.531. Preliminary studies indicate that this provides a resin matrix that has an excellent optical match with many common filler systems. It is also expected that Bis-GMA/BuNCO also can be blended with UDMA to yield resin matrices with refractive indices higher than the 1.480 of UDMA, and thereby improve the optimal optical match with the conventional glass fillers used in current dental composites. This study also suggests that other pendant alkyl urethane modified Bis-GMA monomers also can be used as comonomers with Bis-GMA or UDMA to yield resin systems with higher, more optically suitable refractive indices, lower polymerization shrinkage, higher conversion and reduced water absorption.

Table 1 also shows the degree of vinyl conversion for the urethane modified Bis-GMAs along with Bis-GMA and their mixtures. The degree of vinyl conversion, determined from near infrared spectroscopy, was considerably higher for the urethane-modified Bis-GMAs compared with Bis-GMA. This could be due to relatively weaker hydrogen bonding of urethane groups in the modified Bis-GMA (reflected in their lower viscosities) compared to the stronger hydrogen bonding of the hydroxyl groups of Bis-GMA [11]. The increased mobility in the backbone chain in urethane modified Bis-GMA thus allows for higher vinyl conversion.

As shown in Fig. 2 the viscosities of urethane modified Bis-GMA monomers were significantly lower than those of Bis-GMA. Table 1 also shows zero shear viscosities for urethane-modified Bis-GMA and that of Bis-GMA. The zero shear viscosity of UDMA is 6.75 (0.02). The low viscosities of urethane modified Bis-GMA monomers compared to the stiffer Bis-GMA are attributed to the increase in backbone mobility resulting from the presence of the alkyl pendant substituents from the side chains and the weaker intermolecular hydrogen bonding of the urethane groups compared to the stronger hydrogen bonding interactions of the hydroxyl groups of Bis-GMA.

The values for volumetric shrinkage for Bis-GMA, the urethane modified Bis-GMAs and Bis-GMA mixed with TEGDMA or the butyl urethane modified Bis-GMA are shown in Table 1. The values in parentheses are the average standard deviation of the mean values for n = 3. The lower shrinkage value for Bis-GMA reflects its lower conversion compared to the urethane modified Bis-GMAs. In this study, both shrinkage and vinyl conversion were measured under identical conditions. Polymerization shrinkage of the urethane modified Bis-GMAs would always be lower than Bis-GMA if compared at constant conversion values, e.g. if both are extrapolated to 100% conversion, because of their greater molecular masses.

Measurements of water uptake showed that all the urethane modified Bis-GMA polymers were significantly less hydrophilic than the Bis-GMA polymer. The photo-crosslinked urethane-modified Bis-GMAs reached equilibrium faster compared to Bis-GMA. Furthermore, as the length of the hydrocarbon side chain was increased, the modified Bis-GMAs polymers became increasingly hydrophobic (Fig. 3). This is consistent with the replacement of the hydrophilic hydroxyl groups of Bis-GMA with increasingly hydrophobic substituents.

All modified Bis-GMA polymers (unfilled) had lower flexural strengths compared with that of the Bis-GMA polymer (Table 2). The values in parenthesis represent the standard deviation of the mean, n = 5. Also compared (as shown in Table 2) were the flexural strengths in MPa for a 1:1 mass fraction mixture of Bis-GMA and the butyl urethane modified Bis-GMA (bis-GMA/BuNCO) and that of a 1:1 mass fraction mixture of Bis-GMA and TEGDMA.

Both the length of the hydrocarbon chain, which acts as a flexibilizing substituent, and the moderated hydrogen bonding

Fig. 2. Viscosity as a function of shear rate for the urethane modified Bis-GMAs at 25 °C compared to Bis-GMA and UDMA.

Fig. 3. Water uptake as a function of time for the urethane modified Bis-GMAs compared to Bis-GMA. (Each point represents a mean value of three different determinations; relative standard uncertainty is between 2 and 20%).
interactions of the urethane groups contributes to the lower flexural strengths for these modified Bis-GMA polymers.

Currently we are investigating the use of these and similar urethane modified Bis-GMAs as comonomers for Bis-GMA, UDMA and other base dental resins. This is expected to lead to the development of polymeric dental composites with improved properties compared to similar composites that employ TEGDMA as a comonomer. The combination of low polymerization shrinkage with high vinyl conversion, reduced water uptake, and lower potential tissue penetrability, with potentially enhanced biocompatibility would seem to make these new types of monomers worthy of further investigations.

Acknowledgements

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References


Table 2
Flexural Strength of urethane modified Bis-GMAs compared to Bis-GMA and Bis-GMA/TEGDMA (50:50)

<table>
<thead>
<tr>
<th>Resin</th>
<th>Flexural strength (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bis-GMA</td>
<td>85.9 (13.2)</td>
</tr>
<tr>
<td>Bis-GMA/EnNCO</td>
<td>79.2 (7.2)</td>
</tr>
<tr>
<td>Bis-GMA/PnNCO</td>
<td>55.6 (13.9)</td>
</tr>
<tr>
<td>Bis-GMA/ButNCO</td>
<td>57.6 (4.5)</td>
</tr>
<tr>
<td>Bis-GMA/HexNCO</td>
<td>54.0 (4.9)</td>
</tr>
<tr>
<td>Bis-GMA/OctNCO</td>
<td>47.5 (5.6)</td>
</tr>
<tr>
<td>Bis-GMA/(Bis-GMA/ButNCO) (50:50)</td>
<td>73.7 (14.5)</td>
</tr>
<tr>
<td>Bis-GMA/TEGDMA (50:50)</td>
<td>128.7 (9.4)</td>
</tr>
</tbody>
</table>

The value in parentheses is the average standard deviation of mean value derived from five measurements.