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Preparation and characterization of Bis-GMA-free dental composites with dimethacrylate monomer derived from 9,9-Bis[4-(2-hydroxyethoxy)phenyl]fluorene

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ABSTRACT

Objective. Synthesize a new BPA-free monomer for use in methacrylate-based materials and evaluate critical properties of resin and composite materials based on the monomer.
Methods. Bis-EFMA was synthesized through reaction between 9,9-bis[4-(2-hydroxyethoxy)-phenyl]fluorene and 2-(methacryloyloxy)ethyl isocyanate. Experimental Bis-EFMA-based resin (Bis-EFMA/TEGDMA = 50/50, wt./wt.) and composite were prepared. Critical properties were investigated according to standard or referenced methods Bis-GMA/TEGDMA (50/50, wt./wt.) resin system, Bis-GMA-based composite and 3 M ESPE Filtek™ Z250 were used as controls.
Results. FT-IR and ^{1}H NMR spectra confirmed the structure of Bis-EFMA monomer. Cured resin materials: Bis-EFMA-based and Bis-GMA-based resins had nearly the same degree of conversion ($p > 0.05$); Bis-EFMA-based resin had significantly lower shrinkage, water sorption and solubility, and cytotoxicity than Bis-GMA-based resin ($p < 0.05$); flexural properties of Bis-EFMA-based resin were all higher than those of Bis-GMA-based resin ($p < 0.05$). Cured composite materials: There was no significant difference in conversion ($p > 0.05$); Bis-EFMA-based composite had significantly lower shrinkage and solubility ($p < 0.05$); water sorption of Bis-EFMA-based composite and Z250 were similar ($p > 0.05$), but lower compared to Bis-GMA-based composite ($p < 0.05$); Bis-EFMA-based composite had the deepest curing depth ($p < 0.05$); Before water immersion, there was no significant difference in flexural strength between Bis-EFMA-based composite and each control composite ($p > 0.05$), while FS became lower than that of Z250 ($p < 0.05$), but higher than that of Bis-GMA-based composite ($p < 0.05$) after water immersion; Flexural modulus of Bis-EFMA-based composite and Z250 were nearly the same ($p > 0.05$), higher than that of Bis-GMA-based composite ($p < 0.05$); Bis-EFMA-based composite showed less cytotoxicity than Bis-GMA-based composite and Z250 ($p < 0.05$).

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Significance. Bis-EFMA has potential as a substitute for Bis-GMA to prepare Bis-GMA-free dental composites.

1. Introduction

Bisphenol A (BPA) has been reported as one of many endocrine disrupting compounds [1] which may cause male reproductive abnormalities [2,3], and spermatogenesis impairment [4,5]. Indeed, a waste range of adverse effects have been associated with BPA in animal studies, such as diabetes, obesity, behavioral changes and infertility. A recent report by EFSA (European Food Safety Authority) evaluated the scientific bases for adverse health effects from BPA and concluded that an effect was likely on liver, kidney and breast of rat and mouse [6].

BPA exposure from dental materials has been documented in several studies [7–14], even though BPA itself is not a component in methacrylate-based dental materials. However, these dental materials are manufactured using monomers derived from BPA, such as 2,2-di(4-methacryloxyphenyl)propane (Bis-DMA), 2,2-bis[4-(2′-hydroxy-3′-methacryloyloxy-propoxy)phenyl]propane (Bis-GMA), and ethoxylated Bisphenol-A-dimethacrylate (Bis-EMA). Leaching of BPA may then occur due to BPA-contamination or degradation processes, though some studies have shown that only Bis-DMA can be hydrolyzed into BPA [15–17]. Therefore, monomers that are BPA derivatives, and which are commonly used in methacrylate-based dental composite materials, have become a concern for patients, dentists and manufacturers.

The European committee SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks) recently presented an opinion on the safety of use of BPA in medical devices [18]. The report concluded that the long-term exposure from dental materials was below the temporary value for tolerable daily intake (t-TDI) set by EFSA. Still, the report recommended that medical devices, including dental materials, which do not leach BPA should be preferred when possible, and that the replacement of BPA should be considered. Thus, as a health precaution in order to minimize human exposure to BPA from dental materials, using monomers which are not derived from BPA to prepare dental materials may be effective.

In order to prepare Bis-GMA free dental materials, several new (meth)acrylate monomers such as urethane dimethacrylates [19–21], cycloaliphatic dimethacrylates [22,23], hyperbranched methacrylates [24,25], silicon containing dimethacrylates [26], and fluorinated (meth)acrylates [27–29] have been used as Bis-GMA substituents. Some of these monomers showed significant improvements over Bis-GMA, but others had at least one disadvantage such as lower mechanical properties, or higher water sorption and solubility, when compared with Bis-GMA. In addition to new (meth)acrylate monomers, several new resin systems also have been introduced into dental application, such as oxiranes [30–32], thiol-enes [33–35], styrenic-methacrylate [36], thiol-Michael [37], vinylcyclopropanes [38,39]. However, as many new methacrylate monomers or resin systems have been developed, as a principle, a new Bis-GMA-free dental material should not be prepared at the expense of sufficient material properties.

In this study, a new dimethacrylate monomer, abbreviated Bis-EFMA and derived from 9,9-Bis[4-(2-hydroxyethoxy)phenyl]fluorene(Bis-HEPF), was synthesized with the aim to prepare Bis-GMA-free dental resin and composite. Bis-HEPF was chosen because the rigid molecular structure could act similar to the BPA-core of the structure in Bis-GMA and reinforce the polymer structure. As well, this structure could endow the polymer with high refractive index and low birefringence [40], which would be beneficial for the light transmission in dental composites. The hypothesis of this study was that Bis-EFMA-based dental resin and composite will have similar or better properties when compared with Bis-GMA-based resin and composite. Bis-GMA/Triethylene glycol dimethacrylate (TEGDMA) dental resin was used as a control for the resin material. Bis-GMA/TEGDMA based composite and a commercial dental composite were used as control for the Bis-EFMA-based composite.

2. Materials and methods

2.1. Materials

9,9-Bis[4-(2-hydroxyethoxy)phenyl]fluorene (Bis-HEPF), 2-(Methacryloyloxy)ethyl isocyanate (MEI), camphorquinone (CQ), and dibutyltin dilaurate (DBTL) were purchased from Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan). Bis-GMA, TEGDMA, and dimethyl aminoethyl methacrylate (DMAEMA) were purchased from Sigma-Aldrich Co. (St. Louis, MO, USA). Silanated dental glass fillers (SCHOTT® UltraFine, GM 27884, 9.4% silane, $d_{50} = 0.4\,\mu m$) were purchased from SCHOTT AG (Mainz, Germany). Reference material 3M ESPE Filtek™ Z250 (Z250) was purchased from 3M Co. (St. Paul, MN, USA). L-929 mouse fibroblasts were from European Collection of Authenticated Cell Cultures (ECACC, Public Health, Salisbury, UK). Further substances were purchased from Sigma-Aldrich: fetal bovine serum, dimethyl sulfoxide (DMSO); and the following from Lonza (Verviers, Belgium): phosphate-buffered saline (PBS), cell culture medium: minimal essential medium (MEM), Penicillin/streptomycin, L-glutamine.

2.2. Instrumentation

FT-IR: Model 670, Agilent Technologies, Santa Clara, CA, USA, with gladiator, PIKE Technologies, Madison, WI. NMR: DRX 500, Bruker Co., Billerica, MA, USA. Analytical balance: AE 163, Mettler-Toledo, Columbus OH, USA. Digital caliper: Type 16EX, 0–150 mm, Mahr Gmbh, Esslingen, Germany. Univer-

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