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Influence of chemical structures of benzodioxole-based coinitiators on the properties of the unfilled dental resin

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ABSTRACT

To investigate the influence of chemical structures of benzodioxole-based coinitiator on the initiating reactivity and the mechanical properties of cured samples for the unfilled dental resin, a mixture of 2,2-bis[4-(2-hydroxy-3-methacryloxyprop-1-oxy)phenyl]propane (bis-GMA) and triethylene glycol dimethacrylate (TEGDMA) (70/30 wt.%) was photoinduced by combinations of camphorquinone (CQ) and benzodioxole derivatives. 2-(*N*,*N*-Dimethylamino)ethyl methacrylate (DMEM) was used as control. The kinetics was monitored by a real-time Fourier transformation infrared spectroscopy (FTIR) and the dynamic mechanical analysis was performed on a dynamic mechanical analyzer (DMA). The cytotoxicity property of the cured samples was evaluated by MTT assay in vitro using VERO as reference cell lines. The results indicated that the 4-position phenyl ring substituents of the benzodioxole-based coinitiator had great influence on the initiating reactivity. Incorporating substituents with π electron acceptors in the 4-position of phenyl ring led to the decrease of the rate of polymerization (R_p) of the CQ/benzodioxole derivatives. However, the electron-donating substituents were useful to increase the reactivity. When compared with CQ/amine initiating systems, the combination of CQ and benzodioxole compounds caused lower R_p but the comparable final double bond conversion. All the cured films initiated by CQ/benzodioxole derivatives had almost the same glass transition temperature (T_g) and storage modulus. Indirect cytotoxicity assessment indicated low cytotoxicity of benzodioxole derivatives. These results were very useful for the design of benzodioxole derivatives with satisfactory reactivity and biocompatibility, and are very important for clinical applications.

1. Introduction

Camphorquinone (CQ)/amine photoinitiating system has been widely used in clinical restorative formulation since the introduction of visible-light-activated resin composites [1–3]. As an essential key ingredient for dental formulations, it is generally used to photoinitiate the free radical polymerization of dimethacrylate such as 2,2-bis[4-(2-hydroxy-3-methacryloxyprop-1-oxy)phenyl]-propane (bis-GMA), triethylene glycol dimethacrylate (TEGDMA) or urethane dimethacrylate (UDMA), and form the highly cross-linked network.

Typically, CQ is excited by exposure to 450–500 nm radiation, and then undergoes the electron/proton transfer process with the coinitiator, i.e. tertiary amine, to produce aminoalkyl free radicals [2–4]. The number and reactivity of the generated aminoalkyl free radicals which depend on the chemical structure of the tertiary amines, modulate the early stages of polymerization kinetics, even the physical and mechanical properties of the cured dental resin.

Although tertiary amines, especially tertiary aromatic amines with para electron-donating substituents, are highly effective hydrogen donors, they are both toxic and mutagenic [5]. If other components are essentially non-toxic, the inherent toxicity of the dental resin composites is connected with the mobility of amine molecule. Thus, increasing the size of the amine molecule by incorporating the bulky substituents [6–8] or using the polymerizable amines that contain unsaturated tertiary amine group [9–13], is expected to reduce the diffusion from the resin into the surrounding tissue to a minimum possibility.

Recently, Shi [14–16] and Wang et al. [17] reported that benzodioxole derivatives could be used as potential alternatives to tertiary amines. Unlike the amine coinitiator, benzodioxole derivatives are natural components from dietary plants such as peppers, sesame seeds and carrots [18–20], which are found in a wide variety of human food, essential oils and flavors. They possess antioxidant, antibacterial, antifungal, and other biological activities [19–23]. And no cytotoxic effects of 1,3-benzodioxole derivatives were noticed at a concentration of 10^{-4} M. In particular, the very low mammalian toxicity is of great interest [24]. In this study, three benzodioxole-based compounds were synthesized from

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piperonyl alcohol (PA, a reduction product of a natural component of the extract from black peppers) [18,22] and sesamol (a component of the extract of *Sesamum indicum* L.) [20]. Three synthesized benzodioxole derivatives in combination with PA and benzodioxole (BDO) reported in the previous papers, were used to investigate the influence of electronic effect of the 4-position phenyl ring substituents on the reactivity of the CQ/benzodioxole-based coinitiator system and the properties of dental resin composites. Ethyl 4-*N*,*N*-dimethylaminobenzoate (EDMAB) and 2-(*N*,*N*-dimethylamino)ethyl methacrylate (DMEM) were examined for comparison. The cytotoxicity property was evaluated by MTT in vitro using VERO as reference cell lines.

2. Materials and methods

2.1. Materials

The monomer 2,2-bis[4-(2-hydroxy-3-methacryloxyprop-1-oxy)phenyl]propane (bis-GMA, Aldrich) and triethylene glycol dimethacrylate (TEGDMA, Sartomer) were used as received. Camphorquinone (CQ, Aldrich), 2-(*N*,*N*-dimethylamino)ethyl methacrylate (DMEM), piperonyl alcohol (PA, Acrōs Organics) and sesamol (Acrōs Organics) were used without further purification. Other chemicals were analytical reagents.

2.2. Methods

2.2.1. NMR

^{1}H NMR spectra was recorded on a Bruker AV600 unity spectrometer operated at 600 MHz with TMS as an internal reference, using $CDCl_3$ as the solvent.

2.2.2. FTIR

Real-time FTIR with a horizontal sample holder (Nicolet 5700, Thermo Electron, USA, equipped with an extended range KBr beam-splitter and an MCT/A detector) was used to monitor the extent of polymerization. The mixture of monomer and initiating system was placed in a mold made from glass slides and spacers with 15 ± 1 mm in diameter and 1.2 ± 0.1 mm in thickness. The visible light photopolymerization was triggered by a visible spot light source (EFOS Lite, with 400–500 nm filter and crystal optical fiber that the diameter at the fiber exit was 5 mm, Canada). Light intensity was 100 mW cm^{-2} (400–1000 nm, Beijing Normal University, China). Real-time FTIR data were collected with the resolution of 4 cm^{-1} and 0.3985 s sampling interval. The absorbance change of =C—H peak area from 6101 to 6261 cm^{-1} in the near IR range was correlated to the extent of polymerization. For each sample, the series FTIR runs were repeated three times and the error on the reported double bond conversion as a function of polymerization time was less than 1%.

2.2.3. Synthesis

2.2.3.1. Synthesis of 3,4-methylenedioxybenzene methoxyl acetate (MDBMA). A mixture of 10.50 g (0.0691 mol) of piperonyl alcohol and 7.68 g (0.076 mol) of triethylamine in 150 ml of toluene was dissolved in a three-necked flask equipped with stirrer, thermometer, and dropping funnel. Under cooling (0–5 °C), 5.4 ml (0.076 mol) of acetyl chloride dissolved in 10 ml of toluene were added during 4 h. After the mixture was allowed to stand overnight, the precipitate was filtered off and washed twice with 25 ml toluene. Then the organic phase was extracted with 150 ml of water, 100 ml of 1 N HCl, and 100 ml of 1 N $NaHCO_3$ and dried overnight by Na_2SO_4. Subsequently, the organic phase was evaporated under vacuum to remove the solvent. The slight yellow crude products were further purified by column chromatography (silica gel 200–300 mesh), eluent:ethyl acetate/*n*-hexane 1/3 (wt./wt.). FTIR 2957, 2895 cm^{-1} (CH), 1737 cm^{-1} (C=O). ^{1}H NMR ($CDCl_3$, δ) 2.07 (—CH_3, 3H), 4.98 (—CH_2—OC(=O), 2H), 5.95 (—O—CH_2—O—, 2H), 6.76–6.84 (—benzene, 3H).

2.2.3.2. Synthesis of 3,4-methylenedioxybenzene methoxyl methacrylate (MDBMM). MDBMM was synthesized via the method mentioned above (Section 2.2.3.1). The amounts of PA and methacryloyl chloride were 10.51 g (0.0691 mol) and 7.96 g (0.076 mol), respectively. The slight yellow crude products were purified by column chromatography (silica gel 200–300 mesh), eluent:ethyl acetate/*n*-hexane 1/3 (wt./wt.). FTIR 2977, 2931 cm^{-1} (CH), 1717 cm^{-1} (C=O), 1637 cm^{-1} (=C—H), 811 cm^{-1} (C=C). ^{1}H NMR ($CDCl_3$, δ) 1.94 (—CH_3, 3H), 5.07 (—CH_2—OC(=O), 2H), 5.6, 6.12 (=CH_2, 2H), 5.95 (—O—CH_2—O—, 2H), 6.78–6.85 (—benzene, 3H).

2.2.3.3. Synthesis of sesamol methacrylate (SMA). SMA was synthesized via the method mentioned above (Section 2.2.3.1). The amounts of sesamol and methacryloyl chloride were 9.54 g (0.0691 mol) and 7.96 g (0.076 mol), respectively. The yellow crude products were purified by column chromatography (silica gel 200–300 mesh), eluent:ethyl acetate/*n*-hexane 1/4 (wt./wt.). FTIR 2990, 2896 cm^{-1} (CH), 1734 cm^{-1} (C=O), 1633 cm^{-1} (=C—H), 812 cm^{-1} (C=C). ^{1}H NMR ($CDCl_3$, δ) 2.03 (—CH_3, 3H), 5.73, 5.98 (=CH_2, 2H), 5.97, 6.30 (—O—CH_2—O—, 2H), 6.53–6.78 (—benzene, 3H).

The chemical structures of benzodioxole (BDO), PA, MDBMA, MDBMM and SMA are shown in Fig. 1.

2.2.4. DMA

A dynamic mechanical analyzer (DMA) (Rheometyic, USA) was used to perform the mechanical properties measurement. The samples (three samples for each initiating system) were photocured at room temperature by the same visible light source (light intensity ≈ 500 mW cm^{-2}) for 15 min in a mold made from glass slides and spacers with approximately 1.2 mm thickness and dimensions of 7 mm × 35 mm. The polymerized samples were kept at room temperature for 5 days after curing to ensure that the post-polymerization process was complete. Dynamic mechanical analysis was performed over a temperature range from −50 to 200 °C with a ramping rate of 5 °C per minute using extension mode. The loss and storage modulus and the loss tangent (tan δ, ratio of loss to storage modulus) were recorded as a function of temperature, and the glass transition temperature (T_g) was taken to be the maximum of the loss tangent versus temperature curve.

2.2.5. Methylthiazolydiphenyl-tetrazolium bromide (MTT) assay

The cytotoxicity of the cured films was evaluated based on a procedure adapted from the ISO10993-5 standard test method. VERO cell was cultured in RPMI1640 medium supplemented with 10% fetal bovine serum, together with 1.0% penicillin–streptomy-

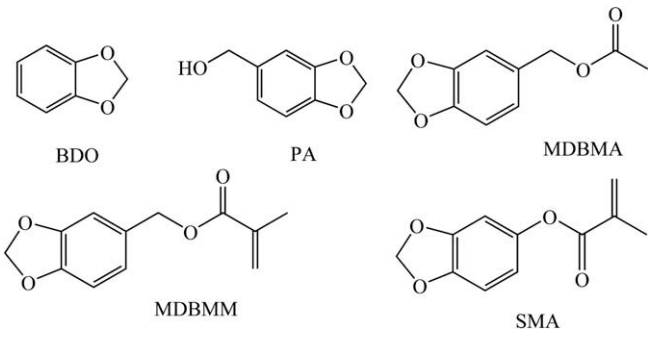

Fig. 1. Chemical structures of BDO, PA, MDBMA, MDBMM and SMA.