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REVIEW ARTICLE

Benzodioxole derivative as coinitiator for dental resin

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Abstract

Objective. The aim of this work was to examine whether it was possible to substitute benzodioxole derivatives for amine as coinitiators for dental application. ***Material and Methods.*** A mixture of urethane dimethacrylate (UDMA)/triethylene glycol dimethacrylate (TEGDMA) (70/30 wt%), camphorquinone (CQ) and coinitiators was photocured. Real time Fourier Transform Infrared Spectroscopy with a horizontal sample holder was used to monitor the extent of polymerization. Dynamic mechanical analysis was performed over a temperature range from $-50^{\circ}C$ to $200^{\circ}C$, with a ramping rate of $5^{\circ}C$ per minute, using extension mode. ***Results.*** Benzodioxole derivatives as coinitiator improved the rate of polymerization and final double bond conversion of the dental resin. The cured samples showed similar properties, e.g. modulus, glass transition temperature, water sorption and solubility. ***Conclusion.*** The results indicate that two benzodioxole derivatives, piperonyl alcohol (PAL) and benzodioxole (BDO), are viable alternatives to conventional amines as coinitiator. The biocompatibility of benzodioxole derivatives makes them more promising than amine in dental resin formulations.

Key Words: *Benzodioxole derivative, camphorquinone, dental resin, photopolymerization*

Introduction

The modern dental resin composites based on dimethacrylates have now been in use in clinical practice for several decades, since Bowen first introduced a resin mixture composed of 2,2-bis [4(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (Bis-GMA) in 1962 [1]. The current commercial resin composites generally contain a mixture of dimethacrylate-based monomer system, a large quantity of inorganic fillers and a photoinitiator system [2]. The photoinitiator system used in dental application is often a CQ-amine couple that generally produces free radicals initiating the photopolymerization of dental formulations and forming a three-dimensional network rapidly [3,4].

The CQ-amine initiating system is a minor but significant component of the resin composite. It greatly influences the reactivity, mechanical properties and biocompatibility of the cured films. However, the unreacted photoinitiator and amine coinitiator, as well as the photolysis products, tend to cause discoloration of the cured composite [5]. In addition, the amine is known to be both toxic and mutagenic [6–12]. In order to decrease toxicity and improve the polymerization process, much work has been done to find a substitute for the amine coinitiator [13–16].

Benzodioxole derivatives, widely found in plant products [17,18], have shown potent antioxidant and antibacterial activities [19,20]. It has recently been reported that 1,3-benzodioxole derivatives possess cytotoxic activity against several human tumor cell lines, including human colon carcinoma cells [21] and multidrug-resistant nasopharyngeal carcinoma cells [22]. No cytotoxic effects were noticed at a concentration of 10^{-4} M [23]. Furthermore, it has been found in previous research that a hydrogen abstraction process can take place from the methylene-bridge carbon of the benzodioxole compound and form a methylenedioxybenzene radical [23]. It is therefore highly likely that benzodioxole derivatives could serve as hydrogen donor for a CQ-based system initiating the photopolymerization of dental composite resin. In this article, three benzodioxole compounds were investigated as coinitiator for a CQ-based photoinitiating system. The effect of concentration and the chemical structures of benzodioxole

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derivatives on the polymerization kinetics and properties of cured polymers was investigated.

Material and methods

Materials

Urethane dimethacrylate (UDMA; Esstech, Essington, Pa., USA) and triethylene glycol dimethacrylate (TEGDMA; Sartomer Chemical Co. West Chester, Pa., USA), with a mass ratio of 70/30, were used as resin matrix. The photoinitiator camphorquinone (CQ) was obtained from Aldrich (Wisc., USA). Ethyl 4-N,N-dimethylaminobenzoate (EDMAB; Aldrich, Wisc., USA) and 2-(dimethylamine)ethyl methacrylate (DMEM; Aldrich, Wisc., USA) were used as amine controls. The experimental coinitiators 1,3-benzodioxole (BDO), 3,4-methylenedioxybenzoic acid (piperonylic acid, PAC) and 3,4-(methylenedioxy)benzyl alcohol (piperonyl alcohol, PAL) were purchased from Acrös Organics (Geel, Belgium). All samples were used as received without further purification. The chemical structures are shown in Figure 1.

Measurement

Real time Fourier Transform Infrared Spectroscopy (Real time FTIR). The mixture of UDMA, TEGDMA, CQ and coinitiator was placed in a mold made from glass slides and spacers 15 ± 1 mm in diameter and 1.2 ± 0.1 mm in thickness. Visible light photopolymerization carried out at room temperature was triggered using an EFOS Lite spot light source (5 mm crystal optical fiber) (EFOS Inc., Mississauga, Canada) with a 400–500 nm filter for 4 min. Light intensity was 100 mW/cm^2 (Beijing Normal University, Beijing, China). Real time FTIR (in a 7000–4000 cm^{-1} spectra range) with a horizontal sample holder (Nicolet 5700; Thermo Electron, Madison, Wisc., USA, equipped with an extended range KBr beam-splitter and an MCT/A detector), was used to monitor the extent of polymerization. Real time FTIR was collected with resolution 4 cm^{-1}. The absorbance change of the =C-H peak area from 6100.70 cm^{-1} to 6220.50 cm^{-1} was correlated to the extent of polymerization. The FTIR runs were performed three times for each sample.

Dynamic mechanical analysis (DMA). The samples, three for each polymer system, were photocured with a visible light at room temperature with a visible light source (EFOS Lite with 400–500 nm filter, light intensity = 500 mW/cm^2) for 10 min in a mold made from glass slides and spacers. The polymerized

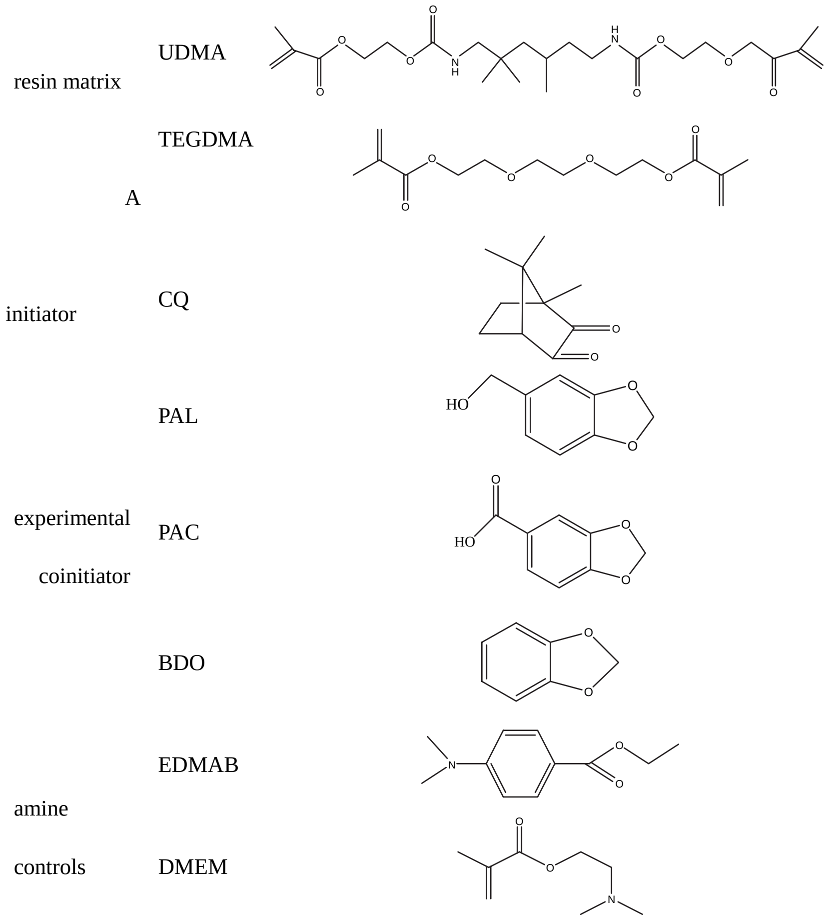

Figure 1. Chemical structure of monomers and photopinitiator systems.

samples were kept at room temperature for 5 days after curing to ensure that the post-polymerization process was completed. The dimensions of samples used for DMA were approximately 7 × 35 × 1.2 mm. Dynamic mechanical analysis was performed over a temperature range from −50°C to 200°C with a ramping rate of 5°C per minute using extension mode. The loss and storage modulus and loss tangent (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.

Water sorption and solubility. Water sorption and solubility were measured in accordance with ISO 4049. Specimens, 15 ± 1 mm in diameter and 1.2 ± 0.1 mm in thickness, were stored in a desiccator containing anhydrous calcium chloride. The samples were maintained at 37 ± 1°C for 24 h. The temperature was then decreased to 23°C for 1 h and the samples subsequently weighed to an accuracy of ± 0.2 mg. This process was repeated until a constant mass m_1 was obtained. The specimens were then immersed in water and maintained at 37°C for 7 days, after which time the samples were removed, washed in water, blotted to remove surface water, waved in the air for 15 s, and weighed 60 s after being removed from the water. This measurement was recorded as m_2. Following weighing, the specimens were again placed in the desiccator and the cycle described previously was repeated until a final constant mass was obtained (m_3). The volumes of the specimens (V) were also measured. The value for each polymer system was the average of five specimens. The following equations were used to calculate water sorption (W_{sp}) and solubility (W_{sl}):

$$Wsp = (m2 - m3)/V \tag{1}$$

$$Wsl = (m1 - m3)/V \tag{2}$$

All samples were cured with a 500 mW/cm^2 visible light source (EFOS Lite with 400–500 nm filter) for 10 min before measurement.

Results

PAL was used to study the concentration of benzodioxole derivative on the kinetics of UDMA/TEGDMA (70/30 wt%). Figures 2 and 3 were the kinetics of UDMA/TEGDMA at the same CQ concentration (0.5 wt%) with different PAL concentrations. The results obtained showed that, even without PAL, CQ alone could initiate the photopolymerization of UDMA and TEGDMA, and lead to a considerable rate of polymerization (R_p). The addition of small amounts of PAL accelerated photopolymerization and brought about increases in the maximum R_p (R_p^{max}, s^{-1}) and in the final double bond conversion (DC), but the decrease in the time in which R_p^{max} appeared (t_{max}, min) (Figures 2a, b and 3a). However, with the increases in the DC, the DC in which R_p^{max} appeared (P_{max},%)

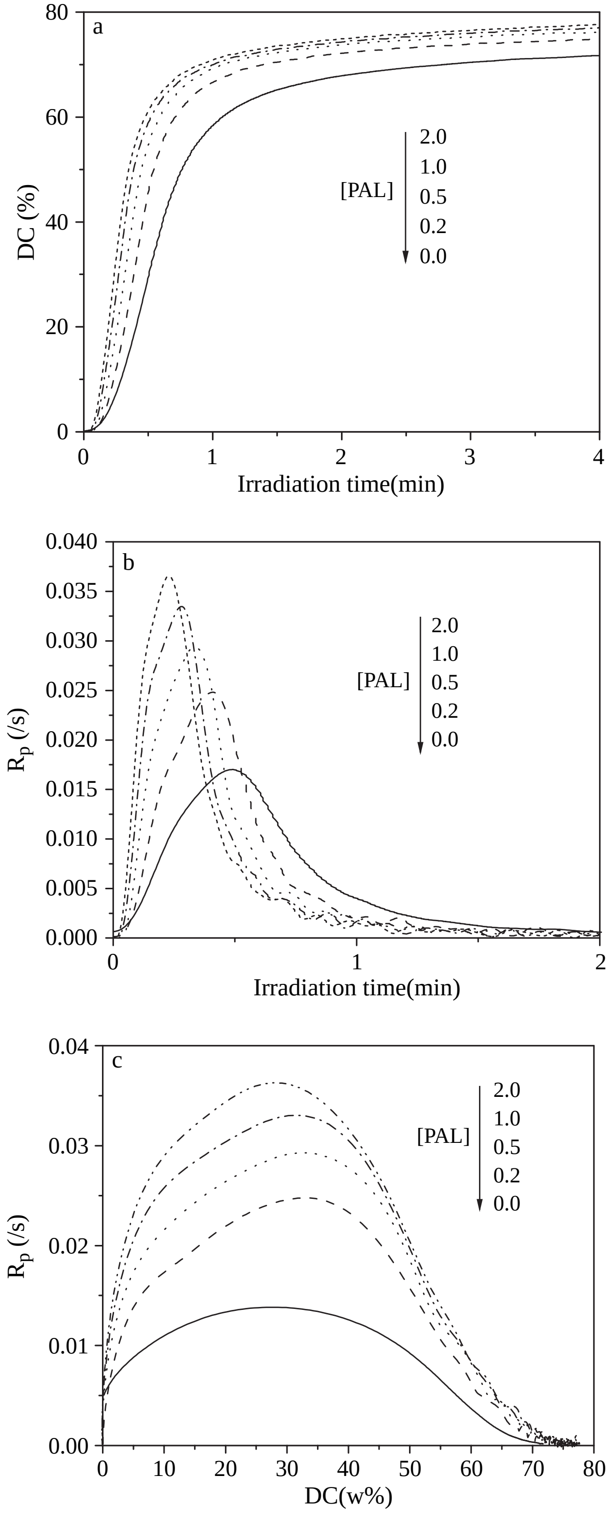

Figure 2. Effect of concentration of piperonyl alcohol on the kinetics of UDMA/TEGDMA (70/30 wt%) with a fixed CQ concentration (0.5wt%) (a) double bond conversion (DC) vs. irradiation time, (b) rate of polymerization (R_p) vs. irradiation time, (c) rate of polymerization (R_p) vs. double bond conversion (DC).

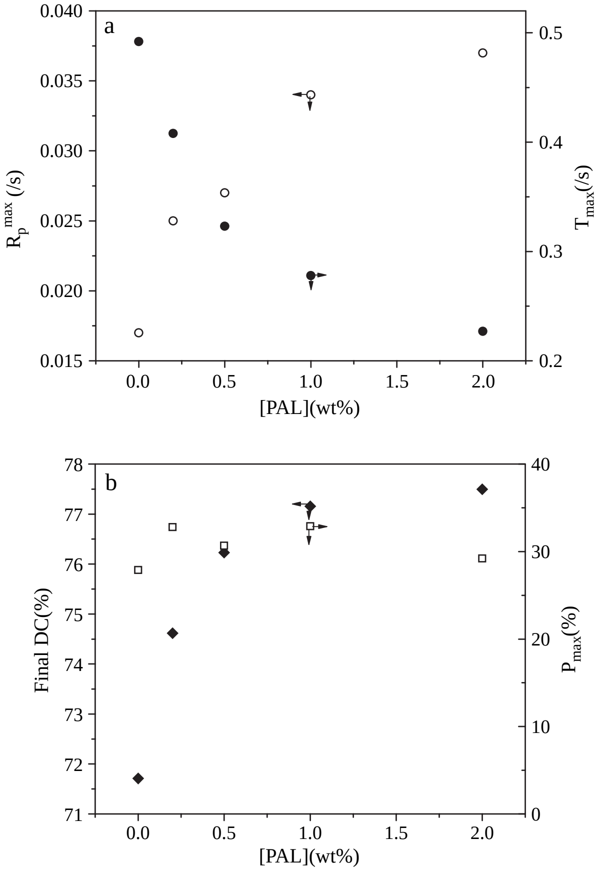

Figure 3. The relationship of concentration of PAL and R_p^{max}, t_{max}, P_{max} and final DC for UDMA/TEGDMA (70/30 wt%) with a constant CQ concentration (0.5 wt%) (a) R_p^{max} (○), t_{max} (●), (b) final DC (◆),P_{max} (□).

was almost insensitive to the concentration of PAL (Figures 2c and 3b).

The kinetics initiated by benzodioxole derivatives and amine controls (EDMAB and DMEM) are compared in Figure 4. Even though the R_p of EDMAB and DMEM was higher than that of the experimental benzodioxole derivatives (PAL, PAC, BDO) (Figure 4b), it was observed that the final DC were very close to each other (around 75%) (Figure 4a).

The storage modulus of experimental benzodioxole derivatives was slightly higher than that of amines, particularly at or near body temperature (37°C) (Figure 5). However, the glass transition temperatures (T_g) of amine controls and experimental benzodioxole derivatives were almost the same (~125°C) (Figure 6), suggesting that the combination of CQ and benzodioxole derivatives could be used as initiator system for dental composite.

Table I gives the results of water sorption and solubility of cured samples initiated by mixtures of 0.5 wt% CQ and 0.5 wt% of different coinitiators. The results indicated that water solubility of the PAL and PAC systems was slightly higher than that of the amine system, but cured samples initiated by different initiator systems brought almost the same water sorption properties. Water sorption and solubility values for all samples were within the range of the ISO 4049 standards.

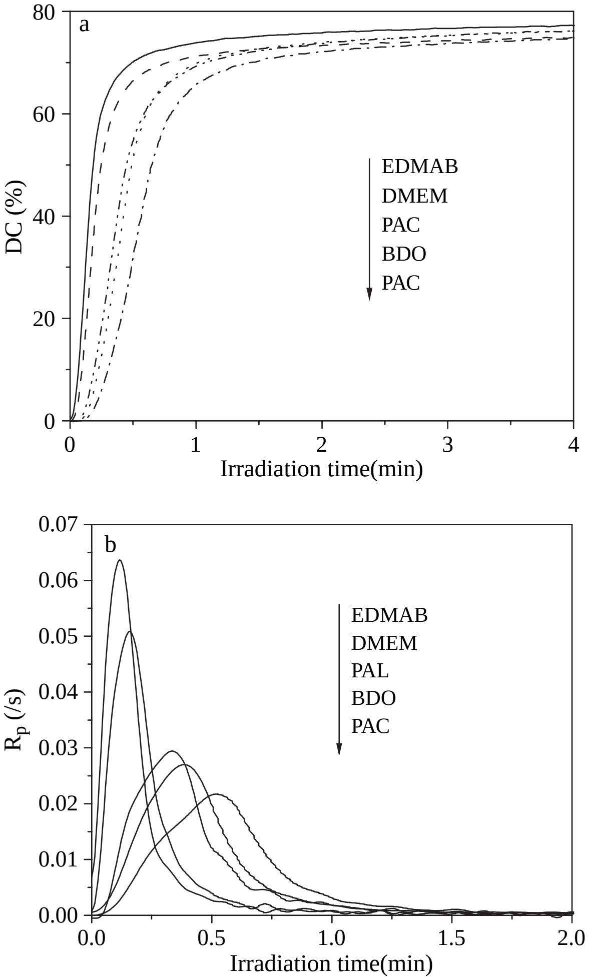

Figure 4. Effect of coinitiators on the kinetics of UDMA/TEGDMA (70/30 wt%) initiated by CQ/coinitiator (0.5/0.5wt%) (a) double bond conversion (DC) vs. irradiation time, (b) rate of polymerization (R_p) vs. irradiation time.

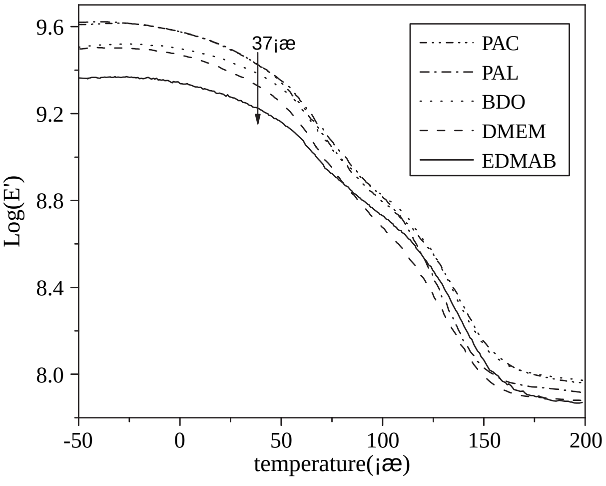

Figure 5. Storage modulus of UDMA/TEGDMA/CQ (0.5 wt%)/Coinitiator (0.5 wt%).

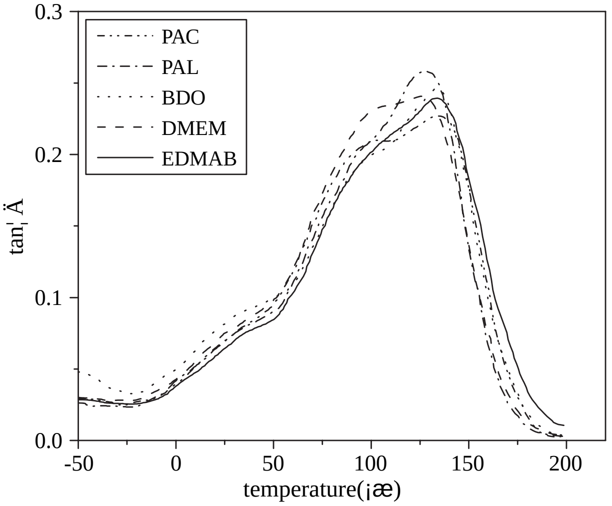

Figure 6. Glass transition temperature of UDMA/TEGDMA/CQ (0.5 wt%)/Coinitiator (0.5 wt%).

Discussion

The real time near FTIR technique is a convenient way of monitoring the decrease in the C–H absorbance peak area for thick (1 mm) photocured samples [24,25]. Upon irradiation, the extent of polymerization is accurately reflected by measuring the decrease in the C–H absorbance peak area as a function of time. The rate of polymerization can be calculated by the time derivative of the DC curve.

For the most commonly used CQ-amine photoinitiating system, the concentration of CQ and coinitiator, as well as the nature of the coinitiator, directly affects the clinical parameters, i.e. curing speed and degree of conversion [3]. Similar to the CQ-amine system, the concentration of PAL greatly influences the kinetics (Figures 2 and 3). The addition of PAL accelerated photopolymerization markedly, indicating that hydrogen abstraction from the methylene-bridge carbon of PAL could occur to form a methylenedioxybenzene radical and initiate the polymerization of UDMA/TEGDMA. The P_{max} is almost insensitive to the concentration of PAL. This might be due to the fact that autoacceleration began at the same DC from the beginning of the polymerization at a different rate of polymerization.

However, amines are known to be both toxic and mutagenic [6–12], and aromatic amines have been noteworthy carcinogens [26,27]. Tertiary aromatic amines have been reported with lower cytotoxicity than primary aromatic amines. When compared with N, N-dimethyl-p-toluidine (DMT), 4-N,N-dimethylaminobenzoic acid (DMAB) and its ethyl ester (EDMAB) as derivatives of p-aminobenzoic acid and ethyl p-minobenzoate have been assumed to show less toxicity in dental application [28].

Table I. Water sorption and solubility of UDMA/TEGDMA (70/30 wt%) initiated by mixtures of 0.5 wt% CQ and 0.5 wt% different coinitiators, mean of five samples (standard derivation).

Initiator System	Water sorption Mean (SD) g/mm^3	Water Solubility Mean (SD) g/mm^3
PAL	41.72 (0.66)	0.57 (0.07)
PAC	42.95 (0.57)	0.61 (0.06)
BDO	40.89 (0.42)	0.49 (0.08)
EDMAB	40.37 (0.39)	0.38 (0.03)
DMEM	39.85 (0.44)	0.39 (0.02)

For small-size initiating systems, the leaching of amine coinitiator would cause potential toxic and carcinogens problems [26,27,29,30]. To improve biocompatibility, polymeric or macromolecular amines have been reported to have significant advantages over commercially available low molecular weight photoinitiators [31,32]. However, the increase in the molecular weight of amines causes the color and solubility problems which limited their application in dental resin [31]. To solve these problems, polymerizable amines emerged as required [33,34]. Incorporation of the unsaturated groups into the structure of tertiary amines could reduce the possibility of its diffusion from the polymer network into the surrounding tissues via co-polymerization with the monomer system [29].

Benzodioxole derivatives as a new kind of synergist for CQ were from dietary plants such as sassafras, nutmeg, carrots, parsley, pepper, and sesame seeds [17,18], which were found in a wide variety of human food, essential oils and flavors. The benzodioxole derivatives in particular had very low mammalian toxicity [18], which rendered them more promising as synergists for CQ in dental applications.

Water sorption and solubility are important parameters for dental composite. Materials with high water sorption and solubility are not suitable for dental composite. The ISO 4049 standards for dental restorative resins are: water sorption (<50 μg/mm^3) and water solubility (<5 μg/mm^3). As indicated in Table I, the water sorption and solubility values for all the cured samples in this study were within the range of the ISO 4049 standards. Since the addition of fillers to the resin matrix would decrease the water sorption and solubility of the composites, benzodixole derivatives are promising coinitiators in dental applications.

Conclusions

The natural component characteristics of benzodioxole derivatives make them promising alternatives to commercial amine as the photoinitiating system for dental resin composite.

Acknowledgments

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