Benzodioxoles as Alternative Coinitiators for Radical Polymerization in a Model-Dental Adhesive Resin

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ABSTRACT: This study evaluated the effectiveness of benzodioxole derivatives as coinitiators of radical polymerization in a model-dental adhesive resin. To compose the adhesive resin, a monomer mixture based on 50 wt % of Bis-GMA, 25 wt % of TEGDMA, and 25 wt % of HEMA was used. Camphorquinone (CQ) 1 mol % was used as a photoinitiator to initiate polymerization. 1,3-Benzodioxole (BDO) and piperonyl alcohol (PA) were used as coinitiators at 0.25, 0.5, 1, 2, 4, 8, and 16 mol % level. In addition, tertiary amine, ethyl 4-dimethylamino benzoate (EDAB) was used as coinitiator in the control group. Some physical, chemical, and mechanical properties of the polymer formed in the experimental adhesives were evaluated using the kinetics of polymerization, sorption and solubility, flexural strength, and elastic modulus tests. The results indicated that BDO and PA were effective coinitiators in the photoinitiator system based on CQ. Comparisons between the benzodioxoles derivative coinitiators and EDAB showed similar performance in the kinetics of polymerization and flexural strength. For water sorption and solubility evaluation, BDO and PA demonstrated significantly more sorption of water and less solubility than the EDAB control group. The findings suggest that BDO and PA were feasible alternatives to conventional amine as coinitiator. © 2012 Wiley Periodicals, Inc. J. Appl. Polym. Sci. 000: 000–000, 2012
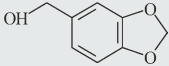
INTRODUCTION

Several photoinitiators have been developed for polymers used in dental materials, and continuing efforts are being made to obtain more efficient photoinitiator systems, exhibiting faster polymerization rates, better photosensitivity, and improved polymer properties.[1–4] The polymerization of visible light-activated dental polymers is generally photoinduced by camphorquinone (CQ)–amine combinations, which have been applied in most of commercial resins.[5,6] CQ (2,3-bornanedione) has 166.22 g/mol molecular weight and an absorption peak around 468 nm.[6] As a type II photoinitiator, CQ requires a coinitiator.[7] The initiation of polymerization occurs through the H-donor radical (R·), whereas the inactive ketyl radical disappears by a radical coupling process.[1] CQ presents low polymerization quantum yield and polymerization efficiency due to the formation of radicals following light absorption and the chain initiation performance of these radicals, which varies with the light source.[8]

The coinitiators most commonly used associated with CQ are tertiary aliphatic or aromatic amines.[6,7] These photoinitiation systems are effectives, generating polymers with adequate mechanical properties.[5,7,9] Moreover, photoinitiators are important to facilitate photopolymerization at the dentin–resin interface, improving the adhesive performance.[10] Contemporary restorations have failed because of deficient pigmentation and marginal sealing.[11–13] Investigations into the longevity,[14–16] biocompatibility, and cytotoxicity of the chemical constituents of adhesive materials have been gaining prominence.[17–19] *In vitro* and *in vivo* studies have demonstrated that adhesive components have cytotoxic effects; nevertheless, these effects could be due to deficient polymerization.[17–19] Amines are also known to form by-products during the photoreaction, causing yellow to brown discoloration under the influence of light and heat.[20]

However, amines are known to be potentially toxic and mutagenic, and aromatics amines have been notable carcinogens.[21–25] From this aspect, it is strategic to investigate components that

Table I. Benzodioxole Derivatives Used

Derivative	1,3-Benzodioxole	Piperonyl alcohol
Molecular formula	$C_7H_6O_2$	$C_8H_8O_3$
Molecular weight	122.121	152.147
Molecular structure		
Synonyms	1,2-(methylenedioxy) benzene	1,3-benzodioxole-5-methanol
		3,4-(methylenedioxy) phenylmethanol
		3,4-(methylenedioxy) benzyl alcohol

could promote improvements in biological characteristics, and maintain good mechanical properties. Coinitiators alternatives to amine have been studied.[4,26,27] Some benzodioxoles present in the human diet are considered as antioxidants, because of their protective action against free radicals produced under oxidative stress associated with their biocompatibility.[28] Benzodioxole derivatives (Table I) are widely distributed in nature and have been shown to have antitumor, radioprotective, cosmetic,[29] antifungal, antibacterial, and many other biological activities.[30]

Considering the promising use of benzodioxole derivatives for methacrylate radical polymerization, the aim of this study was to advance the knowledge about polymer network development according to the type and concentration of benzodioxole derivatives used as coinitiators in a model-dental adhesive resin. The null hypothesis tested was that there would be no differences in the physicochemical and mechanical characteristics of the adhesive resin when compared with the amine-based coinitiator.

METHODS

Reagents
Bisphenol A glycidyl dimethacrylate (Bis-GMA), triethylene glycol dimethacrylate (TEGDMA), 2-hydroxyethyl methacrylate (HEMA), and camphorquinone (CQ) were supplied by Esstech (Esstech, Essington, PA) and used without further purification. The 1,3 benzodioxole (BDO), piperonyl alcohol (PA), and ethyl 4-dimethylamino benzoate (EDAB) were purchased from Aldrich Chemical

Table II. Composition of the Different Binary Photoinitiating System Used in Comparisons of Types of Coinitiator

Composition (mol %)	Adhesive resins (A)		
	A_{BDO}	A_{PA}	A_{EDAB}
Camphorquinone (CQ)	1	1	1
1,3 Benzodioxole (BDO)	4	–	–
Piperonyl alcohol (PA)	–	4	–
Ethyl 4-dimethylamino benzoate (EDAB)	–	–	1
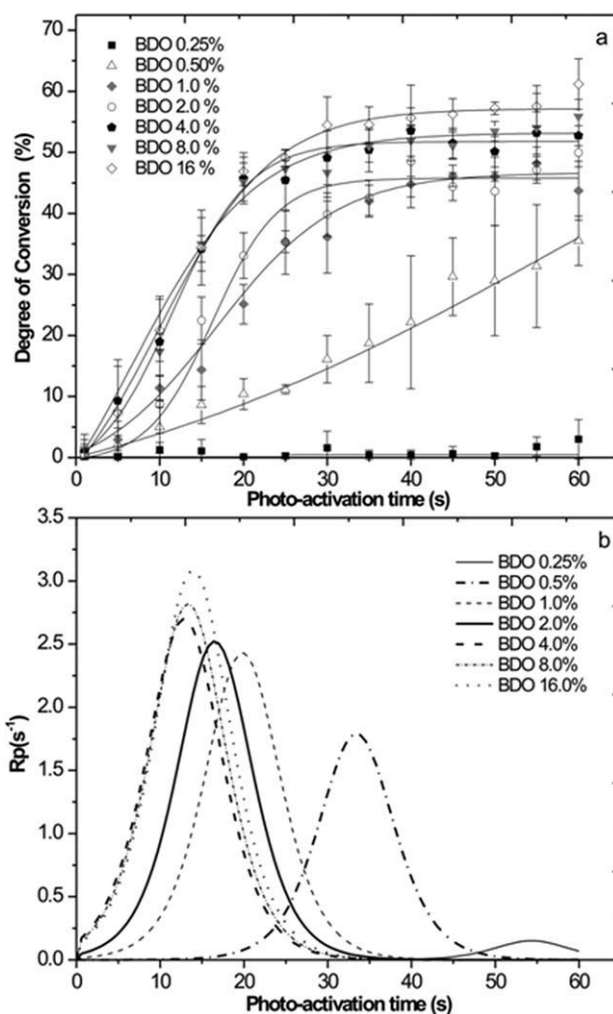
Figure 1. (a) Polymerization kinetics of CQ/BDO (camphorquinone/1,3-benzodioxole), binary photoinitiator system with different amounts of coinitiator; (b) rate of polymerization of the different BDO molar fractions.

(Fluka, Milwaukee, WI) and used without further processing. To perform the monomer light-activation, a quartz-tungsten-halogen light-activation unit (XL 3000, 3M ESPE, St. Paul, MN) was used and the irradiation value (>650 mW/cm^2) was confirmed with a digital power meter (Ophir Optronics, Danvers, MA).

Formulations
A model-dental adhesive resin was formulated by the intensive mixing of 50 wt % Bis-GMA, 25 wt % TEGDMA, and 25 wt % HEMA. CQ was added at 1 mol % for all groups, according to the monomer moles. Three initiator systems were investigated: CQ + BDO, CQ + PA, and CQ + EDAB (Table II). The alternative coinitiators were tested at various molar concentrations: 0.25, 0.5, 1, 2, 4, 8, or 16 mol % of either BDO or PA. The control resin was composed of CQ and 1 mol % of EDAB (a sufficient concentration observed in previous studies).[3,7] No radical scavenger was added to avoid interference with the polymerization kinetics.

Kinetics of Polymerization by RT-FTIR Spectroscopy
The degree of conversion of the experimental adhesive resins was evaluated using real time Fourier Transform infrared spectroscopy
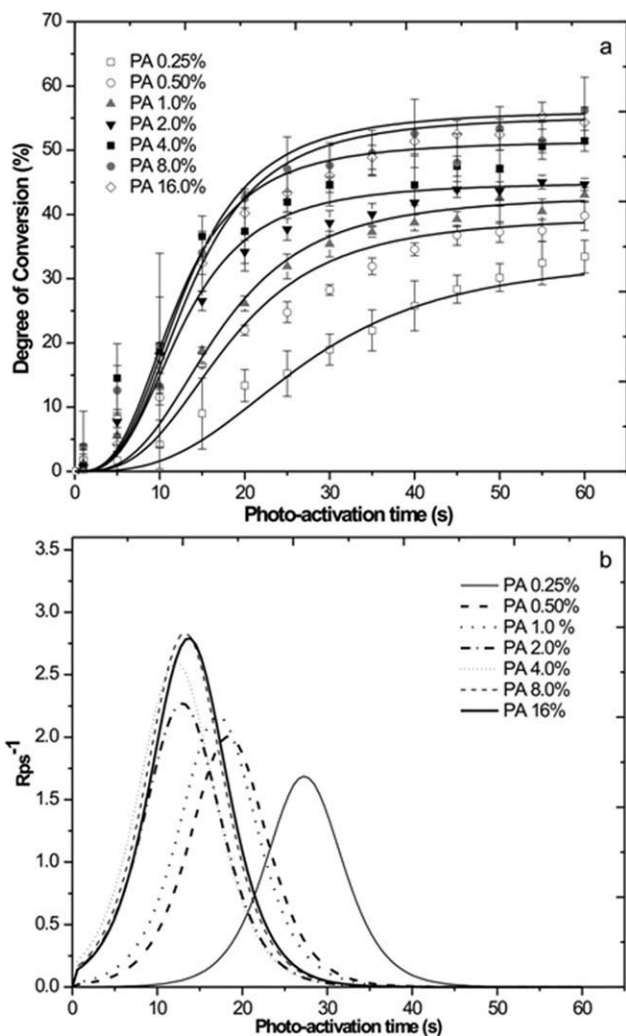
Figure 2. (a) Polymerization kinetics of CQ/PA (camphorquinone/piperonyl alcohol), binary photoinitiator system with different amounts of coinitiator; (b) rate of polymerization of the different PA molar fractions.

(RT-FTIR) with a Shimadzu Prestige21 spectrometer (Columbia, MD) equipped with an attenuated total reflectance device composed of a horizontal ZnSe crystal, with a 45° mirror angle (PIKE Technologies, Madison, WI). A support was coupled to the spectrometer, holding the light-curing unit and standardizing the distance between the fiber tip and the sample at 5 mm.

The IRSolution software (Shimadzu) was used in the monitoring scan mode, using Happ–Genzel apodization, at a range of 1750 and 1550 cm^{-1}, resolution of 8 cm^{-1}, and mirror speed of 2.8 mm/s. With this setup, 1 scan every 1 s was acquired during light-activation.[31] Analysis was performed at a controlled room temperature of 23 ± 1°C and relative humidity <60%. The sample (3 μL) was dispensed directly onto the ZnSe crystal and immediately photo-activated for 60 s. The degree of conversion for each scan was calculated,[3] considering the intensity of carbon–carbon double bond stretching vibration (peak height) at 1635 cm^{-1}, and as an internal standard, the symmetric ring stretching was used at 1610 cm^{-1} from the polymerized and unpolymerized samples. Kinetic of polymerization data were plotted and Hill's three parameter nonlinear regressions were used for

curve fitting. As the coefficient of determination was close to 0.99 for all curves, the rate of polymerization (R_p) was calculated considering the data fitting.[32] For characterization of different concentrations of alternative coinitiators, the data were grouped as shown in Figures 1 and 2. The kinetics and rate of polymerization behavior of groups A_{EDAB}, A_{BDO}, and A_{PA} are illustrated in Figure 3.

Flexural Strength and Elastic Modulus

Flexural strength (σ) and elastic modulus (E) were obtained using a mini-flexural three-point bending test. Ten bar-shaped specimens (10 mm length × 2 mm width × 2 mm height) were made for each resin, using customized stainless-steel molds. The model-dental adhesive resin was placed into the mold, which was placed on top of an acetate strip. The top and bottom surfaces of the specimens were then light-polymerized with two irradiations of 20 s on each side. After polymerization, the specimens were removed from the mold and stored in distilled water at 37 ± 1°C for 24 h. The flexural test was performed in a
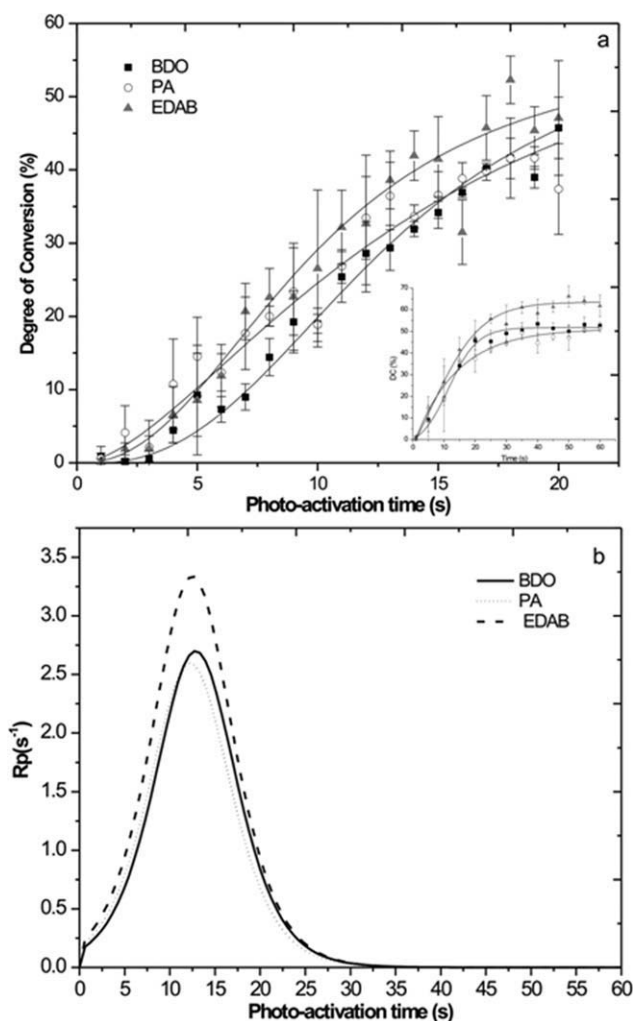
Figure 3. Comparison between the degree of conversion and rate of polymerization of the different binary photoinitiation systems tested: CQ/BDO (camphorquinone/1,3-benzodioxole), CQ/PA (camphorquinone/piperonyl alcohol), CQ/EDAB (camphorquinone/ethyl 4-dimethylamine benzoate).
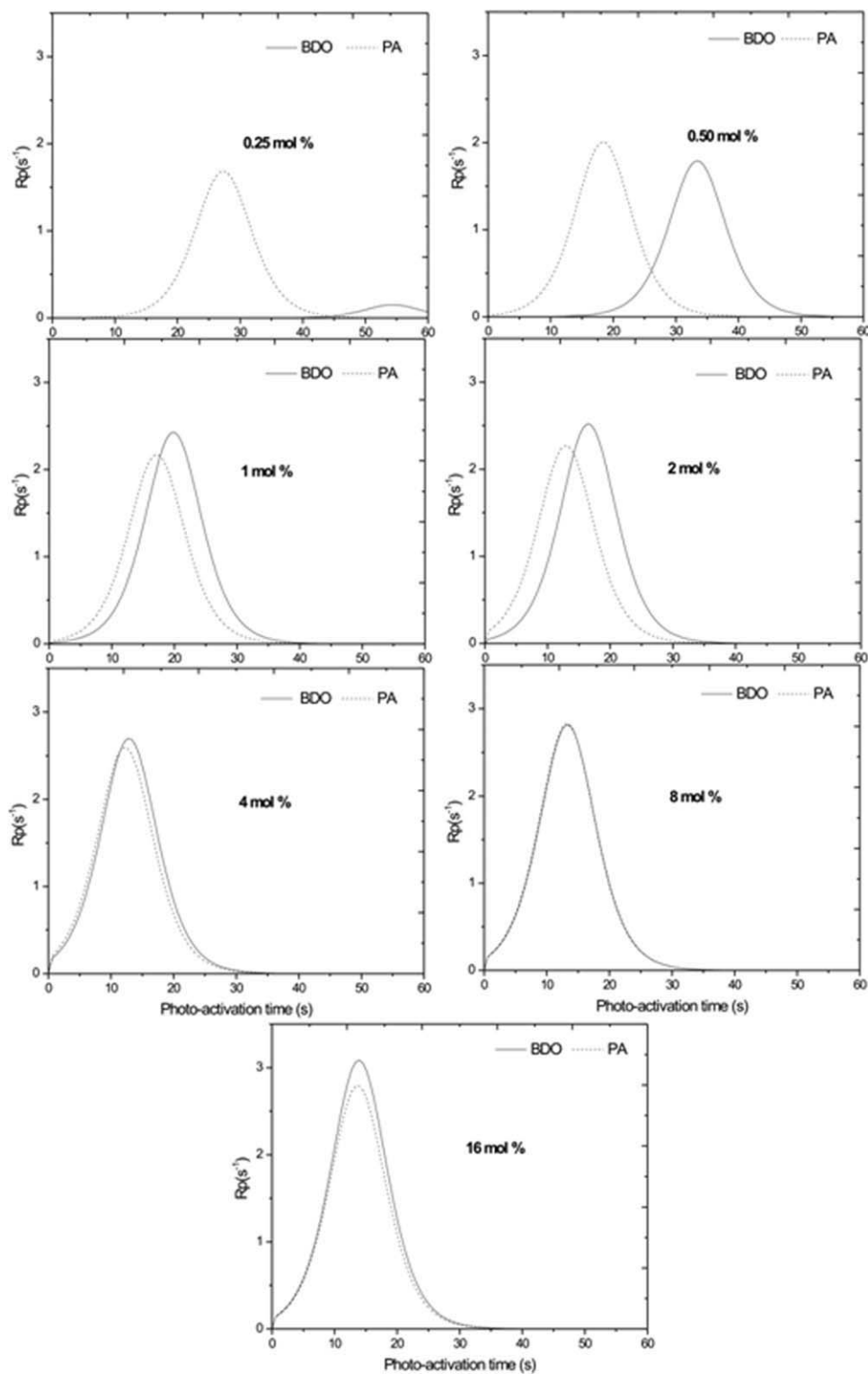
Figure 4. Comparison between the rate of polymerization for screening the concentration of coinitiator proposed for photoinitiator systems based on CQ and benzodioxole derivatives for adhesive resins. Legend: BDO, 1,3-benzodioxole; PA, piperonyl alcohol.

universal testing machine (DL-500, Emic, São José dos Pinhais, Brazil) at a crosshead speed of 0.5 mm/min. The maximum loads were obtained and the (σ) was calculated in MPa using the following formula:

$$(\sigma) = 3FL/(2BH2)$$

The elastic modulus, in GPa, was determined as:
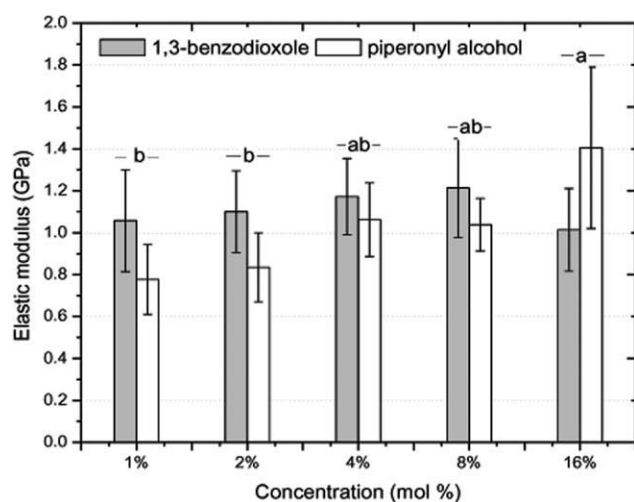
$$E = FL^3/4BH^3 d$$
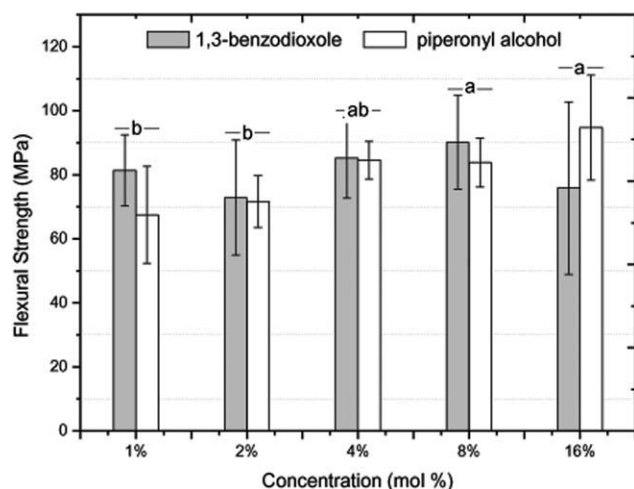
Figure 5. Flexural strength evaluation of the benzodioxoles derivatives coinitiators tested in different concentrations. Different lowercase letters indicate statistical differences according to factor concentration.

where F is the maximum load; L is the length of support span (mm); B is the width of the specimen, H is the height of the specimen, and d is the deflection (mm) corresponding to the load F.

To evaluate the influence of coinitiator type and concentration (factors), the flexural strength and elastic modulus data were submitted to two-way ANOVA (factor concentration and factor coinitiator) and Tukey *post hoc* test for multiple comparisons in different concentrations and coinitiators used. Based on the performance achieved by the groups in the kinetics of polymerization, the flexural strength and the elastic modulus, the coinitiator type comparisons were evaluated as shown in Table II. Data for flexural strength and elastic modulus were submitted to one-way ANOVA and Tukey's *post hoc* test for comparisons with the control.

Water Sorption and Solubility

Water sorption (WS) and solubility (SL) were determined according to ISO specifications 4049/2000. Ten disc-shaped specimens

Figure 6. Elastic modulus evaluation of the different concentrations of benzodioxole derivatives coinitiators tested. Different lowercase letters indicate statistical differences according to factor concentration.

Table III. Flexural Strength and Elastic Modulus of the Adhesive Resins with Different Photoinitiating Systems Evaluated (n = 10) and Standard Deviation (±SD)

Adhesive resin (A)	Flexural strength[a] (MPa)	Elastic modulus (GPa)
A_{BDO}	84.84 (±14.02)	1.19 (±0.19)[A]
A_{PA}	84.57 (±6.20)	1.06 (±0.18)[AB]
A_{EDAB}	74.91 (±15.06)	0.92 (±0.14)[B]

Values followed by different superscript capital letters in columns show statistical differences for photo-initiation system ($P < 0.05$).
EDAB, ethyl 4-dimethylaminobenzoate; BDO, 1,3 benzodioxole; PA, piperonyl alcohol.
[a]There were no statistical differences for adhesive resins ($P < 0.05$).

were fabricated in an aluminum mold between two glass slides covered with polyethylene film. After removing the glass slides, the specimens were light-activated for 20 s on both top and bottom surfaces. Immediately after polymerization, the specimens were placed in a desiccator containing freshly dried silica gel and calcium chloride. After 24 h, the samples were removed, stored in a desiccator at 23°C for 1 h and weighed on an analytical balance with an accuracy of 0.001 mg (AUW 220D, Shimadzu, Kyoto, Japan). This cycle was repeated until a constant mass ($m1$) was obtained. Thickness and diameter of the specimens were randomly measured in five places using a digital caliper (Digimatic Caliper 500-144B, Mitutoyo Sul Americana, Suzano, Brazil) rounded-off to the nearest 0.01 mm, and these measurements were used to calculate the volume (V) of each specimen (in mm^3). The discs were immersed in distilled water at 37°C for 7 days, then removed, blotted dry, and weighed ($m2$). After weighing, the specimens returned to the desiccator and were weighed daily to record a third constant mass ($m3$). For each disc, WS and SL were calculated using the following formulas:

$$\text{WS} = (m_2 - m_3)/V \quad \text{SL} = (m_1 - m_3)/V$$

Data for WS and SL were submitted to one-way ANOVA and Tukey's *post hoc* test for multiple comparisons. The statistical significance for all analysis was established at the 0.05 level of significance.

RESULTS

Kinetics of Polymerization

Figures 1 and 2 show the kinetics of polymerization of experimental adhesive resins at the same CQ concentration (1 mol %)

Table IV. Water Sorption and Solubility of the Experimental Adhesive Resins with Different Photoinitiator Systems Evaluated ($n = 10$) and Standard Deviation (±SD)

Adhesive resin (A)	Water sorption (mg/mm^3)	Solubility (µg/mm^3)
A_{BDO}	92.2 (±2.5)[A]	−0.7 (±0.3)[B]
A_{PA}	93.5 (±2.8)[A]	−0.8 (±0.3)[B]
A_{EDAB}	88.3 (±2.4)[B]	−0.2 (±0.5)[A]

EDAB, ethyl 4-dimethylaminobenzoate; BDO, 1,3 benzodioxole; PA: piperonyl alcohol.
Superscript capital letters indicate differences statistically significant between the groups in a same column.
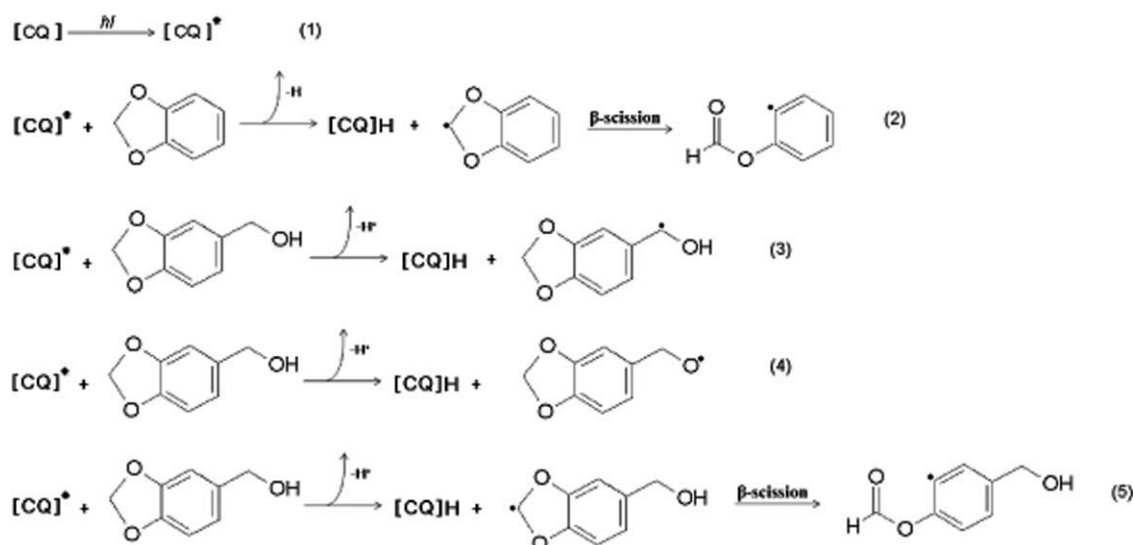
Figure 7. Diagrams 1–5. Photochemical rearrangement mechanism of benzodioxoles derivatives evaluated in this study (1,3-benzodioxole and piperonyl alcohol) with camphorquinone in the experimental adhesive resin.

and different BDO and PA molar concentrations (0.25, 0.50, 1, 2, 4, and 8%). The effects of the concentration and type of the benzodioxole derivative were investigated by the R_p performance, illustrated in Figures 1 and 2. BDO showed smaller effectiveness than PA, at the lower concentrations (0.25 and 0.50%), as indicated by the kinetics and rate of polymerization analysis (Figure 4).

The kinetics of polymerization of the selected concentration (4 mol %) of benzodioxole derivatives coinitiators were compared with those of EDAB (1 mol %) as coinitiator (control group), and are shown in Figure 3. The rate of polymerization showed that the control group presented higher R_p^{max} than the other groups.

Flexural Strength and Elastic Modulus
For flexural strength, only the factor *concentration* was statistically significant ($P < 0.001$) according to two-way ANOVA (Figure 5). Two-Way ANOVA used for comparisons of Elastic modulus showed that the factors *concentration* ($P < 0.001$), *coinitiators* ($P = 0.031$), and *interaction* ($P < 0.001$) were significant. The coinitiator factor (BDO or PA) was significant for the concentrations of 1, 2, and 16 mol %. Comparisons for concentration are demonstrated in Figure 6. No significant differences were detected between concentrations of 1, 2, and 4 molar % regarding flexural strength and elastic modulus. The groups A_{PA} and A_{EDAB} showed similar flexural strength mean (Table III). However, the elastic modulus mean of group A_{BDO} was statistically higher than that of group A_{EDAB} ($P = 0.007$) but similar to that of group A_{PA}, which showed intermediate and statistically similar mean.

Sorption and Solubility
Groups A_{BDO} and A_{PA} showed similar means of sorption and solubility in water according to one-way ANOVA. However, A_{EDAB} demonstrated less sorption and more solubility than the benzodioxole derivatives groups ($P < 0.001$).

DISCUSSION

Infrared spectroscopy is a common method for conversion evaluation,[33] which is a critical issue for methacrylates in dental applications, particularly in the case of dental adhesives. This class of materials is polymerized *in situ*, in an adverse environment, prone to contamination by water, and other biological fluids.[34] Several factors may influence the R_p in radical photoinitiated polymerizations, such as temperature,[35] degree of monomer functionality,[1,36] photoinitiator concentration,[6] coinitiator as well their nature,[37,38] and the effectiveness of the curing light.[8,39]

In the present study, the kinetics of polymerization was remarkably influenced by the concentration of the benzodioxole derivative, irrespective of the type of coinitiator used. As observed in Figure 1(a, b), at 20 s, 0.25 mol % of BDO was unable to promote the initiation of polymerization and 0.5 mol % of BDO obtained an insignificant degree of conversion (10.4%). Observing the calculated R_P data, 0.5% of BDO showed autoacceleration beginning at 15 s and an R_p^{max} of 1.8 s^{-1} at 34 s. To support these findings, it was not possible to obtain solid specimens for the flexural strength and elastic modulus tests. When 1 mol % of BDO was added, a sudden increase in the reactivity of the system was observed with degree of conversion reaching an average of 25%. Autoacceleration started in the initial seconds, reaching an R_p^{max} of 2.4 s^{-1} at 20 s. With 4 mol % of BDO, the effect of concentration on the reactivity was less pronounced, with degree of conversion around 45% and an R_p^{max} occurring between 13 and 16 s. Unlike the low content groups (0.25 and 0.5 mol % concentrations), the formulations of 1 or more mol % were able to produce solid samples. Considering that the benzodioxole derivatives groups with 4 mol % at 20 s reached a degree of conversion (Figures 1 and 2) and flexural resistance (Figures 5 and 6) similar to those of the higher BDO and PA concentrations and of the EDAB performance at 1 mol % (Figure 3 and Table III), this benzodioxole concentration was chosen for water sorption and solubility analysis.

Table IV shows that there were significant differences in water sorption and solubility evaluation among the BDO, PA, and EDAB groups, demonstrating that the benzodioxole groups presented more sorption than the EDAB one, but less solubility. According to Ferracane,[40] the presence of polar chemical groups in the polymer increases its hydrophilicity, and consequently, the sorption of water. The PA has a hydroxyl in its molecule and the 1,3-benzodioxole has an ether linkage, thus contributing to the sorption phenomenon. In contrast with the sorption results, BDO and PA, which not differed statistically, were less soluble than the EDAB group. This can be explained by the significant effect of the cross-link density and the network parameter on the hygroscopic behavior of the polymer.[32]

Regarding to the polymerization reactivity, PA appears to be more effective in promoting initiation than BDO at low concentrations of 0.25 and 0.5 mol %, where is possible to observe a degree of conversion of 13.3 and 22%, respectively at 20 s of light-activation time. This can be explained by the hypothetical mechanism showed in Figure 7, where three possible pathways of radical formation in the PA coinitiator are depicted (Figure 7—diagrams 3, 4, and 5). Similar results were also obtained using PA as coinitiator.[28] However, for the other higher concentrations shown in Figure 4, the efficiency of BDO and PA was similar, indicating that a minimum concentration of BDO to initiate the polymerization was reached. Furthermore, in the action mechanism of the PA, there are three donation possibilities (Figure 7), but it seems that there is a competition in the proton donation, explaining why PA kinetics and rate of polymerization are similar to the BDO.

Studies determining the minimum concentration of CQ and EDAB,[7,41] which causes maximum polymerization, minimum shrinkage stress, and sufficient depth of cure have been reported.[7] It is known that when low-amine concentrations are present (<0.1 wt %), the rate of radical formation is independent of the amine concentration, while for intermediate concentrations (between 0.1 and 0.5 wt %) the rate of radical formation was independent of the amine concentration and dependent only on the amine reactivity.[42] Therefore, the concentration of amine and CQ used in this study could be considered high enough. In addition, the concentration of CQ and amine had to be as low as possible in clinical situations, because of the yellowness and the tendency to internal discoloration of the resin.[38]

CONCLUSION

BDO and PA were shown to be effective coinitiators for dental adhesive resins light-activated by halogen light, being comparable with the conventional amine EDAB, presenting similar physical and mechanical characteristics. BDO and PA presented more sorption of water than EDAB, but less solubility. Moreover, the characteristic of BDO and PA being natural components makes them promising alternatives as photoinitiating systems for dental biomaterials, indicating that some biological improvements in dental adhesive resins could be obtained using benzodioxole derivatives as coinitiators. However, more in-depth evaluations and long-term analyses are necessary to investigate the polymer properties, shelf life, the bond strength, and the hybrid layer characterization.

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