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Effect of Partition of Photo-initiator Components and Addition of Iodonium Salt on the Photopolymerization of Phase-Separated Dental Adhesive

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Abstract

The polymerization kinetics of physically separated hydrophobic- and hydrophilic-rich phases of a model dental adhesive have been investigated. The two phases were prepared from neat resin containing 2-hydroxyethyl methacrylate (HEMA) and bisphenol A glycerolate dimethacrylate (BisGMA) in the ratio of 45:55 (wt/wt). Neat resins containing various combinations of popular photo-initiating compounds, e.g., camphorquinone (CQ), ethyl 4-(dimethylamino)benzoate (EDMAB), 2-(dimethylamino)ethyl methacrylate (DMAEMA) and diphenyliodonium hexafluorophosphate (DPIHP) were prepared. To obtain the two phases 33 wt% of deuterium oxide (D₂O) was added to the neat resins. This amount of D₂O exceeded the miscibility limit for the resins. The concentration of each component of the photo-initiating system in the two phases was quantified by HPLC. When combined with CQ, DMAEMA is less efficient as a co-initiator compared to EDMAB. The addition of DPIHP as the third component into either CQ/EDMAB or CQ/DMAEMA photo-initiating systems leads to comparable performance in both the hydrophobic- and hydrophilic-rich phases. The addition of the iodonium salt significantly improved the photopolymerization of the hydrophilic-rich phase; the hydrophilic-rich phase exhibited extremely poor polymerization when the iodonium salt was not included in the formulation. The partition concentration of EDMAB in the hydrophilic-rich phase was significantly lower than that of DMAEMA or DPIHP. This study indicates the need for a combination of hydrophobic/hydrophilic photosensitizer and addition of iodonium salt to improve polymerization within the hydrophilic-rich phase of the dental adhesive.

Keywords

photosensitizer; co-initiator; iodonium salt; photopolymerization; dentin adhesive; hydrophilic-rich phase

Introduction

Dental restorative composites are too viscous to bond directly to the tooth and thus, lower viscosity dental adhesives must be used to link the composite to the acid-etched enamel and dentin [1]. The dental adhesive infiltrates the wet, demineralized dentin matrix to form a hybrid layer. The composition of the hybrid layer is primarily water, solvent, isolated mineral particles, collagen fibrils and adhesive resin of variable composition along the length and depth of the adhesive/dentin (a/d) interface [2, 3]. Ideally, the adhesive should completely seal the collagen fibrils and thus, protect the collagen from the harsh, oral environment. This ideal is not achieved because infiltration of the resin is incomplete leaving behind exposed collagen fibrils underneath the hybrid layer [3, 4]. The exposed collagen undergoes degradation by host-derived matrix metalloproteinases (MMPs) and such degradation could contribute to the failure of the a/d bond [5]. The durability of the adhesive seal is compromised by several factors including water sorption leading to plasticization, hydrolytic/enzymatic degradation of the adhesive and sub-optimal polymerization [6-10]. Phase separation of the adhesive as it infiltrates the wet, collagen matrix also has a detrimental impact on the integrity of the a/d bond [2, 11].

During infiltration, dental adhesive undergoes phase separation into hydrophobic-rich and hydrophilic-rich phases (Figure 1). A previous investigation quantified the components of methacrylate-based dental adhesive in the hydrophilic-rich phase [12]. The earlier study showed that the hydrophobic cross-linker and the widely used photo-initiator system, such as camphorquinone (CQ) and ethyl 4-(dimethylamino)benzoate (EDMAB), were present in limited concentrations. This could compromise the photo-polymerization of hydrophilic-rich phase and also result in loosely cross-linked regions facilitating diffusion of the oral fluid into the a/d interface [12]. Wang and colleagues showed decreasing concentration of the cross-linker along the depth of the a/d interface [13]. Sub-optimal polymerization and the ingress of oral fluid through the loosely cross-linked regions make the hydrophilic-rich domain vulnerable to hydrolytic and enzymatic degradation, paving the way for infiltration of noxious agents including *Streptococcus mutans* and other cariogenic bacteria at the composite/tooth interface.

Little is known about the characteristics of the hydrophilic domain arising as a result of phase separation. Detailed characterization studies of this phase have been very limited [14-16]. It was found that the polymerization efficiency of the hydrophilic-rich phase mimic is lower as compared to the hydrophobic-rich phase mimic [14]. The polymerization mechanism of the hydrophilic-rich phase involves polymerization-induced and solvent-induced phase separation [15]. It was also observed that methacrylate-based hydrophilic dental adhesive resins having composition very similar to that of the hydrophilic-rich phase mimics, show sub-optimal photo-polymerization at low light intensities; the sub-optimal photo-polymerization was overcome by adding iodonium salt to the formulation [16]. The incorporation of iodonium salt significantly improved the polymerization efficiency but this also led to the formation of shorter polymer chain lengths [16]. Another study by Besse et al. showed that the addition of iodonium salt does not always result in higher polymerization efficiency. For example, in the case of methacrylate phosphonic acids, the iodonium salt had a reverse effect [17].

The results from a study by Park et al. showed that the incorporation of iodonium salt within the hydrophobic/hydrophilic photo-initiating system enhanced the degree of conversion, glass transition temperature and rubbery modulus of dental adhesive formulations that have a composition similar to the hydrophobic-rich phase [18]. The impact of partition of the photoinitiator components and iodonium salt on the photopolymerization of the different phases, especially, the hydrophilic-rich phase, has remained unexplored. The focus of this study is to determine the impact of partitioning of the widely used photosensitizer (camphoquinone) and co-initiators (hydrophobic EDMAB and hydrophilic DMAEMA) on the photo-polymerization of hydrophobic-rich and hydrophilic-rich phase mimics. We also investigated the impact of iodonium salt on the rate of polymerization and degree of conversion of the phases. In previous studies, mimics were prepared with compositions similar to hydrophobic-rich and hydrophilic-rich phases while in this investigation, physically separated hydrophobic-rich and hydrophilic-rich phases were created.

Materials and Methods

Preparation of physically separated hydrophobic-rich and hydrophilic-rich phase

2-hydroxyethyl methacrylate (HEMA), bisphenol A glycerolate dimethacrylate (BisGMA), camphoquinone (CQ), ethyl 4-(dimethylamino)benzoate (EDMAB), 2-(dimethylamino)ethyl methacrylate (DMAEMA) and diphenyliodonium hexafluorophosphate (DPIHP) were obtained from Sigma Aldrich, Milwaukee, WI, USA. For the preparation of the formulation, at first various combinations of photo-initiator systems (Table 1) were added to HEMA, then the solution was vortexed until the photo-initiators dissolved. BisGMA was added, such that the HEMA to BisGMA ratio was 45:55 wt%. The photo-initiators were added 0.5 wt% each based on the total weight of the solution. This control formulation containing 45:55 wt% of HEMA and BisGMA (HB45NR) represents the primary composition of many commercially available dental adhesive resins [19].

The hydrophobic-rich and hydrophilic-rich phases were prepared by adding 33 wt% of deuterium oxide (D₂O, Cambridge Isotope Laboratories Inc., Andover, MA, USA) to the control formulation. This resulted in a cloudy mixture since 33 wt% of D₂O was above the miscibility limit for this formulation [14]. Then, the photo-initiators were replenished based on the quantity of D₂O added so that the final composition of each photo-initiator reached 0.5 wt%. The mixture was vortexed and centrifuged at 10,000 rpm for 20 min to separate it into two distinct liquid layers of hydrophobic-rich and hydrophilic-rich phases. The top layer (lighter hydrophilic-rich phase) was collected carefully using a pipette. Next, the interphase between the two layers was removed. The bottom layer, the hydrophobic-rich phase, was also collected with a pipette. The schematic in Figure 2 shows the preparation technique for the two phases and Table 1 exhibits the composition of each mixture before collection of the two phases by centrifugation. The hydrophobic-rich and hydrophilic-rich phases, obtained in this manner, were used to conduct the polymerization kinetics study.

For high performance liquid chromatography (HPLC), control formulation containing only 0.5 wt% of one of the photo-initiator components was prepared. Then, hydrophobic-rich and hydrophilic-rich phases were obtained using the technique described above. This provided a simplistic approach of identifying and quantifying the photo-initiator components within

hydrophobic-rich and hydrophilic-rich phases. After dilution with HPLC grade ethanol (Acros Organics), each phase solution was filtered using Millipore centrifuge filter device (Ultrafree®-CL, UFC4LCCOO 5000 NMWL, Millipore, Bedford, MA) and a centrifuge (Eppendorf MiniSpin Plus, Eppendorf, Hamburg, Germany) at 10,000 rpm.

Photopolymerization kinetic study

Photopolymerization kinetics study was carried out separately for the hydrophobic-rich and hydrophilic-rich phases in the case of each photo-initiator combination (Table 1). The photopolymerization of the hydrophobic-rich phase was monitored in-situ for 1 hr, and for the hydrophilic-rich phase for 2 hrs. This study was carried out using PerkinElmer Spectrometer Frontier (PerkinElmer, Waltham, MA, USA). A time-resolved spectrum collector was used to monitor the polymerization kinetics with a resolution of 4 cm⁻¹ at ATR sampling mode [15, 16]. At first, 30 µl of the sample was placed on the ATR crystal. Then a plastic cover slip was placed on it. The edges of the coverslip were sealed using tape to prevent evaporation of D₂O from the sample; D₂O evaporation could cause variation in the polymerization kinetics [14, 15]. The D₂O profile was also monitored to ensure that there was no evaporation of D₂O and the initial slight changes in the profile could be related to diffusion, either away from or towards the ATR crystal, within the sample [15]. The band ratio intensities for C=C at 1637 cm⁻¹ to C=O at 1716 cm⁻¹ was monitored and the equation below was used to calculate the degree of conversion (DC).

$$DC = \left(1 - \frac{\text{Absorbance}_{1637\text{cm}^{-1}}^{\text{sample}} / \text{Absorbance}_{1716\text{cm}^{-1}}^{\text{sample}}}{\text{Absorbance}_{1637\text{cm}^{-1}}^{\text{monomer}} / \text{Absorbance}_{1716\text{cm}^{-1}}^{\text{monomer}}} \right) \quad (1)$$

The rate of polymerization was determined taking the differentiation of the DC versus time curve. This was carried out in Microcal Origin (Version 6.0, Microcal Software, Northampton, MA). D₂O was used instead of water (H₂O) to avoid overlap of spectral features of aliphatic C=C with that of H₂O.

High Performance Liquid Chromatography (HPLC)

To quantify the partition concentration of the photo-initiators (EDMAB, DMAEMA, DPIHP) in the hydrophobic-rich and hydrophilic-rich phases, 20 µl of each diluted phase was injected onto the HPLC column with a constant column temperature at 40°C. EDMAB, DPIHP and DMAEMA were quantified in each phase of the adhesive. CQ was not quantified for this study since CQ was not stable in either phase. The major components of the adhesive, BisGMA and HEMA, were not quantified for the two phases since this was determined in a previous study from our group [12]. An isocratic method was employed to quantify EDMAB and DMAEMA in the two phases. For this method the mobile phase consisted of 65 v% acetonitrile (Fisher Scientific) and 35 v% of 10 mM potassium phosphate buffer at a pH of approximately 6.9, which was prepared in house using HPLC grade water (Fisher Scientific). The flow rate for the mobile phase was maintained at 0.5 ml/min. After 24.99 min, the mobile phase was ramped linearly to 85 v% of acetonitrile and kept constant for 5 min. The hydrophobic-rich phase for each photo-initiator component was

diluted 120 times to carry out the HPLC. The hydrophilic-rich phase was diluted 60 times for DMAEMA. In the case of EDMAB, the hydrophilic-rich phase was not diluted.

A Shimadzu LC-2010 CHT HPLC system (Shimadzu, Columbia, MD) was used and it was equipped with a SPD-M20A photo diode array detector, an autosampler with EZstart chromatography software as a controller and for data processing. Separation was performed on a reverse-phase column (Phenomenex Luna 5 μ m C18 4.6 $\times$ 250, Torrance, CA). The photo-initiator components were identified based on their elution time and their concentrations were quantified by comparing the UV absorption intensity at 208 nm against known standards. Hydrophobic-rich and hydrophilic-rich phases from neat resin without any photo-initiator (PI) were also prepared. These phases were diluted to the same level as the corresponding phases prepared from neat resins containing DMAEMA or EDMAB. The chromatograms for the diluted phases without the PIs were subtracted from the chromatogram of the corresponding diluted phases containing one of the PI components (DMAEMA or EDMAB). This allowed more accurate quantification of the absorption intensity for the PI component. The peaks were baseline corrected before the subtraction. This was done using OriginPro (Version 8.0, OriginLab, Northampton, MA). The range of linearity for EDMAB was 5-100 μ g/ml and 10-100 μ g/ml for DMAEMA. The linear relation between intensity and concentration of DMAEMA and EDMAB are given below:

$$\text{Intensity}=4.045[\text{DMAEMA}] - 4.392 \quad R^2=0.99 \quad (2)$$

$$\text{Intensity}=3.183[\text{EDMAB}]+2.893 \quad R^2=0.99 \quad (3)$$

The partition concentrations for DPIHP in both phases were determined by HPLC (Shimadzu LC-2010 CHT HPLC system, Shimadzu, Columbia, MD) but, in this case, a gradient method was employed. The mobile phase was buffer (10 mM phosphate buffer) and acetonitrile but the buffer was ramped linearly from 75 v% to 35 v% in 20 minutes. It was maintained at 35 v% for another 5 minutes before ramping it linearly to 75 v% again in 1 minute which was maintained for another 19 minutes. The gradient method allowed better separation of DPIHP which overlapped with HEMA when the isocratic method discussed above was used. The hydrophobic-rich phase was diluted 20 times and the hydrophilic-rich phase 15 times. The intensity of the DPIHP was determined by subtracting the chromatogram of the phases without any PI (diluted to the same level) from the chromatograms for the corresponding phases containing DPIHP (Figure 6(c) and (d)). Before subtraction the peaks were baseline corrected. The linear relation for intensity and DPIHP concentration is given below and the range for linearity in this case is 95-413 μ g/ml.

$$\text{Intensity}=3.465[\text{DPIHP}] - 2.264 \quad R^2=0.99 \quad (4)$$

Statistical Analysis

The polymerization kinetic study for each PI combination in each phase was carried out in triplicate. For each component in each phase, HPLC was also carried out in triplicate. The

DC and rate maxima were compared for various PI combinations for both hydrophobic-rich and hydrophilic-rich phases by one way ANOVA ($p < 0.05$) and t-Test ($p < 0.05$) using Microcal Origin (Version 6.0, Microcal Software, Northampton, MA). The concentration of PI components determined by HPLC were compared for each phase by one way ANOVA ($p < 0.05$) and t-Test ($p < 0.05$) using Microcal Origin.

Results

Photopolymerization kinetics study

The hydrophobic-rich phase for formulations with EDMAB/DPIHP and DMAEMA/DPIHP exhibited a poor degree of conversion (DC). This result indicated the importance of photosensitizer in triggering the formation of free radicals. The rate of polymerization for these hydrophobic-rich phases was also significantly lower compared to those with CQ/EDMAB, CQ/DMAEMA/DPIHP and CQ/EDMAB/DPIHP (one way ANOVA, t-Test, $p < 0.05$). Poor polymerization and low rate maxima were also observed for both the hydrophobic-rich and hydrophilic-rich phases in the case of PI combination CQ/DMAEMA. The hydrophobic-rich phase for the formulations containing CQ/EDMAB, CQ/EDMAB/DPIHP and CQ/DMAEMA/DPIHP showed a significantly higher degree of conversion and rate maxima compared to the other formulations such as CQ/DMAEMA, CQ/DPIHP, EDMAB/DPIHP and DMAEMA/DPIHP (one way ANOVA, t-Test, $p < 0.05$). The DC for the hydrophobic-rich phase in the case of formulations containing CQ/EDMAB/DPIHP was significantly higher compared to that for the CQ/EDMAB and CQ/DMAEMA/DPIHP (t-Test, $p < 0.05$). The DC for the hydrophobic-rich phase containing CQ/EDMAB and CQ/DMAEMA/DPIHP was statistically similar. There was no statistically significant difference in the rate maxima for the hydrophobic-rich phase containing CQ/EDMAB and CQ/EDMAB/DPIHP (t-Test, $p < 0.05$). Figure 3 shows the representative results from the kinetic study for the hydrophobic-rich phase and Table 2 summarizes the average DC and rate maxima for the hydrophobic-rich phase.

The hydrophilic-rich phase for the formulations containing EDMAB/DPIHP and DMAEMA/DPIHP showed no polymerization. Poor polymerization was observed for the hydrophilic-rich phase in the case of formulations with CQ/EDMAB and CQ/DMAEMA, but the addition of DPIHP to these formulations significantly increased the DC and rate maxima (one way ANOVA, t-Test, $p < 0.05$). The hydrophilic-rich phase for PI combination CQ/DPIHP showed poor DC and the DC was significantly lower than the corresponding hydrophobic-rich phase (t-Test, $p < 0.0001$). There was a statistically significant difference in the DC and the rate maxima for CQ/DPIHP hydrophilic-rich phase compared to the corresponding phases of CQ/EDMAB and CQ/DMAEMA (one way ANOVA, t-Test, $p < 0.05$). The DC and rate maxima for the hydrophilic-rich phase with CQ/DMAEMA/DPIHP was higher than that containing CQ/EDMAB/DPIHP. Figure 4 shows representative results from the kinetic study and Table 3 summarizes the average DC/rate maxima for the hydrophilic-rich phase. Although the kinetic study was monitored for 2 hrs in the case of the hydrophilic-rich phase, Figure 4(a) shows the kinetics results for the first hour only. There was no significant change in DC beyond 1 hr.

High Performance Liquid Chromatography (HPLC)

The concentration of EDMAB and DPIHP was significantly higher in the hydrophobic-rich phase compared to DMAEMA (one way ANOVA, t-Test, $p < 0.05$). Figure 5 shows the chromatogram for the hydrophobic-rich/hydrophilic-rich phases of DMAEMA and EDMAB. In the hydrophilic-rich phase, the concentration of DPIHP was significantly higher than DMAEMA, but the concentration of EDMAB was significantly lower as compared to the other two components (one way ANOVA, t-Test, $p < 0.05$). Figure 6 shows the chromatogram for DPIHP in the hydrophobic-rich/hydrophilic-rich phases and Table 4 summarizes the partition concentration for the 3 components in the hydrophobic-rich and hydrophilic-rich phases. Table 4 also exhibits the partition ratio for the 3 PI components in the hydrophilic-rich phase. The partition ratio for EDMAB in the hydrophilic-rich phase was very low.

Discussions

The reaction mechanism for CQ/tertiary amine, CQ/ tertiary amine /DPIHP and CQ/DPIHP had been proposed by Cook et al. [20]. According to Cook and colleagues, for the CQ/DPIHP system, CQ, after being promoted to the excited state, reacts with the monomer to generate ketyl and alkyl radicals [20]. The ketyl radicals are oxidized by the iodonium salt to regenerate CQ and phenyl radicals. The latter is active in initiation. The reaction between the excited CQ and the monomer is slow and reversible which could explain the lower degree of conversion for both of the phases in case of PI combination CQ/DPIHP when compared to the photoinitiating systems containing a tertiary amine as a co-initiator. The hydrophobic CQ could partition in lower concentration within the hydrophilic-rich phase resulting in the formation of less radicals compared to the corresponding hydrophobic-rich phase. Moreover, the concentration of the monomers is much higher in the hydrophobic-rich phase than the hydrophilic-rich phase [12], which could make the latter less reactive. The possibility of the excited CQ reacting with the monomers to produce ketyl and alkyl radicals could be very low for the hydrophilic-rich phase.

In the case of the system containing CQ/tertiary amine, electron transfer from an amine to the excited CQ results in the formation of photo-induced electron transfer (PET) species [20]. This is a reversible reaction. Proton transfer within PET results in aminoalkyl and ketyl radicals, where the former is active in initiation and the latter takes part in the termination reaction [20]. HPLC results suggested that EDMAB was present in very low concentrations in the hydrophilic-rich phase and CQ, being hydrophobic, could also be present in low concentrations in this phase. This could lead to the generation of radicals in insufficient quantities within the hydrophilic-rich phase and result in poor photopolymerization of this phase for the PI combination CQ/EDMAB. The HPLC study also exhibited the presence of DMAEMA in higher concentration within the hydrophilic-rich phase compared to EDMAB. CQ could be in lower concentration in this phase for the CQ/DMAEMA formulation, resulting in sub optimal degree of conversion. It is also possible that for the hydrophilic-rich phase, back electron transfer within PET decreases the quantity of free radicals further.

The concentration of DMAEMA was significantly higher (t-Test, $p < 0.05$) within the hydrophobic-rich phase as compared to the corresponding hydrophilic-rich phase (Table 4).

The degree of conversion (DC) of the hydrophobic-rich phase was, however, still sub-optimal for CQ/DMAEMA. The DC for the hydrophobic-rich phase for CQ/DMAEMA was also significantly lower than that for the corresponding CQ/EDMAB formulation. One reason for the sub-optimal DC of the hydrophobic-rich phase for CQ/DMAEMA could be due to the lower concentration of DMAEMA in this phase (Table 4). It is also possible that back electron transfer within PET is higher when DMAEMA is used as the co-initiator, leading to the generation of fewer radicals. The polymerization kinetic result indicates that DMAEMA is less efficient as a co-initiator compared to EDMAB. The following shows the PET formation when electron transfer from DMAEMA to excited CQ takes place and back electron transfer occurs in the reverse direction which causes a decrease in the radical generation [20].

According to Cook et al., the ketyl and aminoalkyl radicals both undergo oxidation by DPIHP generating phenyl radicals [20]. This could cause a decrease in the back electron transfer within PET and increase the generation of radicals. Moreover, replacement of the terminating ketyl radical with phenyl radicals, which is active in initiation, leads to an overall increase in the generation of radicals taking part in the initiation. For the hydrophilic-rich phase, the addition of DPIHP may cause a substantial decrease in the back electron transfer which could result in a higher degree of conversion despite low concentrations of CQ and/or EDMAB in the hydrophilic-rich phase. This could account for the 20.1% and 32.2% average DC seen in the case of the hydrophilic-rich phase containing CQ/EDMAB/DPIHP and CQ/DMAEMA/DPIHP respectively. This could also cause the hydrophilic-rich phase to have a significantly higher rate maxima for CQ/EDMAB/DPIHP and CQ/DMAEMA/DPIHP when compared with their corresponding formulations without DPIHP. The increase in effective radicals could also explain the significantly higher degree of conversion in the case of the hydrophobic-rich phase for CQ/EDMAB/DPIHP and CQ/DMAEMA/DPIHP when compared with their corresponding formulations without DPIHP.

For CQ/DMAEMA/DPIHP, results from the HPLC study showed that DMAEMA was present in higher concentrations within the hydrophilic-rich phase than EDMAB. This could result in a higher degree of conversion and rate of polymerization for the hydrophilic-rich phase containing CQ/DMAEMA/DPIHP as compared to the CQ/EDMAB/DPIHP. Moreover, it is also possible that DPIHP can have higher impact on reducing back electron transfer in the case of DMAEMA than for EDMAB. This is noticeable when the DC values in hydrophobic-rich phases for CQ/EDMAB/DPIHP and CQ/DMAEMA/DPIHP are compared with their corresponding formulations without DPIHP. In the case of the hydrophobic-rich phase containing CQ/DMAEMA/DPIHP, the impact of DPIHP on the polymerization efficiency was higher compared to the corresponding formulation with CQ/EDMAB/DPIHP. This is because the hydrophobic-rich phase containing CQ/DMAEMA showed poor polymerization and the addition of DPIHP increased it substantially whereas the DC values of the hydrophobic-rich phases for CQ/EDMAB and CQ/EDMAB/DPIHP were comparable. It should also be noted that the concentration of DMAEMA in the hydrophobic-rich phase is lower compared to EDMAB (Table 4). Despite this concentration

difference, the DC of this phase for the two co-initiators is comparable when they are used in combination with DPIHP.

The efficiency of the photo-initiating system is an important factor to consider in the design and development of dentin adhesives. The combination CQ/DMAEMA did not lead to substantial DC in either the hydrophobic-rich or hydrophilic-rich phase. Hence, DMAEMA is less efficient as a co-initiator compared to EDMAB, as discussed above. However, if DMAEMA is used along with DPIHP, its performance in the hydrophobic-rich and hydrophilic-rich phases becomes comparable to that of CQ/EDMAB/DPIHP.

This study indicates that the combination of CQ/DMAEMA or CQ/EDMAB is neither an efficient photo-initiating system for at least one of the phases or for both of the phases. This study also indicates that the addition of DPIHP has a significantly positive impact on the photopolymerization especially, for the hydrophilic-rich phase. Despite the positive impact of DPIHP, the DC of the hydrophilic-rich phase was still sub-optimal primarily because the photosensitizer, CQ and/or co-initiator EDMAB was present in insufficient quantity. Therefore, in addition to DPIHP, incorporation of a combination of not only hydrophobic and hydrophilic photosensitizer, but also hydrophobic and hydrophilic co-initiator could lead to substantial polymerization of the hydrophilic-rich phase. Abedin et al. showed that the combination of hydrophobic and hydrophilic photosensitizers, CQ and QTX respectively, along with EDMAB, resulted in a substantial degree of conversion of dental adhesive hydrophilic-rich phase mimic when present in reduced concentration, whereas the combination of only hydrophobic components (CQ and EDMAB) led to poor polymerization at low concentration [14].

In our previous investigation with hydrophilic-rich phase dental adhesive mimics [14, 15], a secondary rate maxima was found but no such secondary stage polymerization was observed for the physically phase separated dental adhesive hydrophilic-rich phase in this study. It was reported previously that BisGMA was present within the physically separated hydrophilic-rich phase in minor quantities, approximately 302 µg/ml which could be much lower than the quantity present in the hydrophilic-rich phase dental adhesive mimics [12]. The presence of the hydrophobic cross-linker in very low concentration within the physically phase separated hydrophilic-rich phase could impair the formation of microgels and hence entrapment of radicals for triggering the secondary rate maxima.

Conclusion

This study shows that the addition of iodonium salt to the adhesive formulation could significantly increase the degree of conversion within the hydrophilic-rich phase. It is suggested that in addition to incorporating iodonium salt, combination of hydrophobic/hydrophilic efficient photosensitizer and co-initiator could lead to enhanced degree of conversion of this phase. However, the hydrophilic-rich phase with substantial degree of conversion will still remain as a vulnerable region for failure due to inadequate cross-linking density. It is expected that this could be overcome by partially incorporating a hydrophilic cross-linker along with a hydrophobic cross-linker such as BisGMA. Therefore, it is possible

to improve the clinical lifetime of the adhesive with appropriate design of water compatible efficient photosensitizers, co-initiators and cross-linkers.

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Figure 1. Phase separation of adhesive during infiltration of the resin through the demineralized dentin giving rise to hydrophobic- and hydrophilic-rich phase

Figure 2.
Schematic showing preparation of hydrophobic-rich and hydrophilic-rich phases of dental adhesive.

Figure 3.

Polymerization kinetics study of hydrophobic-rich phase (a) Degree of conversion (b) Rate of polymerization. The rate maxima for CQ/DMAEMA, DMAEMA/DPIHP and EDMAB/DPIHP are not shown because they are substantially lower than that of the other formulations.

Figure 4. Polymerization kinetics study of hydrophilic-rich phase (a) Degree of conversion (b) Rate of polymerization.

Figure 5.

Chromatograms obtained by isocratic method (Acetonitrile 65 v% and buffer 35 v%). Chromatogram for DMAEMA in the (a) hydrophobic-rich and (b) hydrophilic-rich phases before subtraction of the chromatogram for corresponding phases without containing any PI. Chromatogram for EDMAB in the (a) hydrophobic-rich and (b) hydrophilic-rich phases before subtraction of the chromatogram for corresponding phases without containing any PI. The phases have been diluted by ethanol.

Figure 6. Chromatogram obtained by gradient method. Chromatogram for DPIHP in the (a) hydrophobic-rich and (b) hydrophilic-rich phases before subtraction of the chromatogram for corresponding phases without containing any PI. Chromatogram showing the peak for DPIHP in the (c) hydrophobic-rich and (d) hydrophilic-phases after subtraction of the chromatogram for corresponding phases without containing any PI.

Table 1
Composition of each components in the resin mixture prior to collection of the two phases by centrifugation

Name of Formulation	wt% of BisGMA	wt% of HEMA	wt% of D ₂ O
EDMAB/DPIHP	36.56 ± 0.04	29.94 ± 0.04	33.50 ± 0.08
DMAEMA/DPIHP	36.46 ± 0.25	29.96 ± 0.21	33.58 ± 0.46
CQ/DPIHP	36.33 ± 0.09	30.14 ± 0.07	33.54 ± 0.16
CQ/DMAEMA	36.61 ± 0.04	29.97 ± 0.03	33.42 ± 0.07
CQ/EDMAB	36.70 ± 0.01	30.02 ± 0.02	33.28 ± 0.03
CQ/DMAEMA/DPIHP	36.52 ± 0.06	29.89 ± 0.05	33.59 ± 0.11
CQ/EDMAB/DPIHP	36.59 ± 0.03	29.94 ± 0.02	33.48 ± 0.04

* CQ, EDMAB, DMAEMA, DPIHP were added at 0.5 wt% of the total weight of the mixture

Table 2
Degree of conversion and rate maxima for hydrophobic-rich phase

Formulation Name	Degree of Conversion (DC) after 1 hr	Rate Maxima (s^{-1}) $\times 10^2$
EDMAB/DPIHP	0.068 ± 0.009	0.52 ± 0.02
DMAEMA/DPIHP	0.045 ± 0.013	0.45 ± 0.02
CQ/DPIHP	0.267 ± 0.006	1.64 ± 0.15
CQ/DMAEMA	0.104 ± 0.008	0.77 ± 0.11
CQ/EDMAB	0.771 ± 0.007	8.07 ± 1.37
CQ/DMAEMA/DPIHP	0.747 ± 0.029	16.1 ± 2.1
CQ/EDMAB/DPIHP	0.878 ± 0.007	9.74 ± 0.45

Table 3
Degree of conversion and rate maxima for hydrophilic-rich phase

Formulation Name	Degree of Conversion (DC) after 1.5 hr	Rate Maxima (s^{-1}) $\times 10^4$
CQ/DPIHP	0.087 ± 0.027	46.4 ± 8.4
CQ/DMAEMA	0.024 ± 0.001	13.8 ± 3.9
CQ/EDMAB	0.028 ± 0.018	13.9 ± 10.1
CQ/DMAEMA/DPIHP	0.322 ± 0.034	142 ± 16
CQ/EDMAB/DPIHP	0.201 ± 0.082	94.3 ± 33.1

* The formulations containing EDMAB/DPIHP and DMAEMA/DPIHP did not polymerize

Table 4
Partition concentration of DMAEMA, DPIHP and EDMAB in hydrophobic- and hydrophilic-rich phase

Photo-initiator Component	Content in Hydrophobic-rich Phase (wt%)	Content in Hydrophilic-rich Phase (wt%)	Partition ratio (h'philic / h'phobic)
DMAEMA	0.492 ± 0.003	0.251 ± 0.004	0.510
DPIHP	0.698 ± 0.007	0.286 ± 0.003	0.410
EDMAB	1.063 ± 0.026	0.007 ± 0.000	0.007