A review of the development of radical photopolymerization initiators used for designing light-curing dental adhesives and resin composites

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This paper reviews our recent studies on radical photopolymerization initiators, which are used in the design of light-curing dental adhesives and resin composites, by collating information of related studies from original scientific papers, reviews, and patent literature. The photopolymerization reactivities of acylphosphine oxide (APO) and bisacylphosphine oxide (BAPO) derivatives, and D,L-camphorquinone (CQ)/tertiary amine were investigated, and no significant differences in degree of conversion (DC) were found between BAPO and CQ/amine system ($p > 0.05$). In addition, a novel 7,7-dimethyl-2,3-dioxobicyclo[2.2.1]heptane-1-carbonyldiphenyl phosphine oxide (DOHC-DPPO=CQ-APO) was synthesized and its ultraviolet and visible (UV-VIS) spectral behavior was investigated. CQ-APO possessed two maximum absorption wavelengths ($\lambda_{\max}$) at 350–500 nm [372 nm (from APO group) and 475 nm (from CQ moiety)], and CQ-APO-containing resins exhibited good photopolymerization reactivity, excellent color tone, relaxed operation time, and high mechanical strength. It was also found that a newly synthesized, water-soluble photoinitiator (APO-Na) improved adhesion to ground dentin.

Keywords: Radical photopolymerization, Photoinitiator, Light-curing dental adhesive

INTRODUCTION

Photopolymerization science and technology have assumed in recent years an increasing relevance in many applications¹. In particular, the adverse biological effects of ultraviolet light on vital tissues² have caused visible light-induced radical polymerization to gain fast acceptance in dentistry.

Since an advanced radical polymerization initiator is an extremely valuable component of light-curing dental adhesives and resin composites, numerous studies have tirelessly explored and sought for more advanced photoinitiators.

By virtue of its outstanding performance for light-curing resins in dentistry, D,L-camphorquinone (CQ)/tertiary amine system has hitherto been recognized as a valuable visible light initiator since its invention by Dart and Nemcek³ in 1971. On the initiation mechanism, CQ [wavelength of maximum absorbance ($\lambda_{\max}$): 468 nm] undergoes a so-called hydrogen abstraction type of photoinitiation mechanism in which CQ (a sensitizer) absorbs light to form a photoexcitation complex (CQ*-amine exciplex) with a tertiary amine (a hydrogen-donating agent) and subsequently generates amine-derived free radicals⁴.

Acylphosphine oxide (APO) and bisacylphosphine oxide (BAPO) derivatives have received considerable attention because of their inherently interesting photochemistry and photophysics and because they are widely employed as photoinitiators in free radical polymerization processes of photoradiation industries⁵, and they have recently gained new attention in dentistry.

Unlike the CQ system, APO and BAPO do not

require tertiary amines. They undergo a so-called α -cleavage type of photoinitiation mechanism (Norris type I system)^{6,6}, in which APO undergoes homolytic α -cleavage of the C-P bond and generates two free radical species, *i.e.*, $[-(O=C)\cdot]$ and $[\cdot P(=O)<]$, both capable of initiating polymerization. In terms of curing performance, APO- and BAPO-containing resins cured with a violet light-emitting diode (LED) had approximately the same or higher degree of conversion (DC) when compared against a CQ-containing resin cured with a dental quartz-tungsten-halogen light curing unit⁷. However, APO exhibits poor photoinitiation reactivity with dental blue LED (420–510 nm, $\lambda_{\max}$: 455 nm) because of its wavelength region.

To date, a photoinitiator which contains both α -diketone $[-C(=O)-C(=O)-]$ and acylphosphine oxide $[>P(=O)-C(=O)-]$ groups bound intramolecularly is unknown. In our recent study⁸, a novel CQ derivative bearing an APO group, *i.e.*, 7,7-dimethyl-2,3-dioxobicyclo[2.2.1]heptane-1-carbonyl-diphenylphosphine oxide (DOHC-DPPO=CQ-APO) was synthesized. Its spectral behavior and photopolymerization reactivity were assessed to investigate its potential applicability in the design of light-curing resin composites.

With regard to water-soluble initiators, it is known that water-reactive *tri-n*-butylborane (TBB) initiator^{9,10} enabled hydrophobic methyl methacrylate (MMA) to adhere strongly to moist adherends. To expect the initiation performance like TBB initiator, another noteworthy design consideration is a water-soluble visible light photoinitiator, notably, 2-hydroxy-3-(3, 4-dimethyl-9-oxo-9H-thioxanthen-2-yloxy)-*N*, *N*, *N*-trimethyl-1-propanaminium chloride (QTX). Effects of

Table 1 Abbreviations of materials and methods used in this review paper

Materials: CQ: D,L-camphorquinone, APO: acylphosphine oxide, BAPO: bisacylphosphine oxide, BDPO: benzoyl-diphenylphosphine oxide, TMMPO: 2,4,6-trimethylbenzoyl-methoxy-phenylphosphine oxide, TMDPO: 2,4,6-trimethylbenzoyl diphenylphosphine oxide, PBDPO: phthanoyl-bis(diphenylphosphine oxide), TfBDPO: tetrafluoroterephthanoyl-bis(diphenylphosphine oxide), DFDPO: 2,6-difluorobenzoyl-diphenylphosphine oxide, NDPO: (1-naphthoyl) diphenylphosphine oxide, IC 819 (Irgacure 819) [=TMMPO]: bis(2,4,6-trimethylbenzoyl)-phenylphosphine oxide, IC 1800 (Irgacure 1800): [A: bis(2,6-dimethoxybenzoyl)-2,4,4-trimethyl-pentylphosphine oxide, B: 1-hydroxy-cyclohexyl-phenyl-ketone; A:B=1:3], BCBPO: bis(2,6-dichlorobenzoyl)-(4-propylphenyl)-phosphine oxide, DOHC-DPPO = CQ-APO: 7,7-dimethyl-2,3-dioxobicyclo[2.2.1]heptane-1-carbonyldiphenyl phosphine oxide, CQ-COOH: 7,7-dimethyl-2,3-dioxobicyclo[2.2.1]heptane-1-carboxylic acid, KA: D, L-ketopionic acid, CQ-COCl: 7,7-dimethyl-2,3-dioxobicyclo[2.2.1]heptane-1-carboxylic acid chloride, MDPP: methoxydiphenylphosphine, PPD: 1-phenyl-1,2-propaediene, BCBPO: bis(2,6-dichlorobenzoyl)-(4-propylphenyl)phosphine oxide, Tin-Lau: dibutyltin dilaurate, UDMA: dimethacryloyloxyethyl-2,2,4-trimethylhexamethylene diurethane, TMPT: trimethylolpropane trimethacrylate, QTX: 2-hydroxy-3-(3, 4-dimethyl-9-oxo-9H-thioxanthen-2-yloxy)-N, N, N-trimethyl-1-propanamin-ium chloride, EDAB: ethyl *p*-N,N-dimethylaminobenzoate, PIDAA: N-phenyliminodiacetic acid, DMAEM: N,N-dimethylaminoethyl methacrylate, BSNa: benzenesulfonic acid sodium salt, BPE: 2,2-bis(4-methavryloyloxyethoxyphenyl)propane, MTYA: N-methacryloyltyrosine amide, 10-MDP: 10-methacryloxydecyl dihydrogen phosphate, HEMA: 2-hydroxyethyl methacrylate, GM: glycerol monomethacrylate, GMR: glycerol dimethacrylate, GAM: glycerol methacrylate acrylate, TMDO-Na (= APONa): sodium 2,4,6-trimethylbenzoyl-phenylphosphine oxide, 6-MHPA: 6-methacryloyloxyhexyl phosphonoacetate, TEGDMA (=3G): triethyleneglycol dimethacrylate, p-TSNa: *p*-touluenesulfonic acid sodium salt, CE-6: 18-crown-6-ether, 4-META: 4-methacryloyloxyethyltrimellitic anhydride, 4-AET: 4-acryloyloxyethyltrimellitic acid, 4-MET: 4-methacryloyloxyethyl trimellitic acid, 4-AETA: 4-acryloyloxyethyltrimellitic anhydride, Bis-GMA: 2,2'-bis[4(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (= bisphenol A diglycidylmethacrylate), DMPP: dimethoxy-phenylphosphine, VBPO: 4-vinylbenzoyl diphenylphosphine oxide, DMVBPO: 2,6-dimethyl-4-vinylbenzoyl-diphenylphosphine oxide, TMBVPO: 2,4,6-trimethylbenzoyl(phenyl-4-vinylphenyl)-phosphine oxide, NVP: N-vinylpyrrolidone, DAM: dimethylacrylamide, VBPO: *p*-vinylbenzyl-diphenylphosphine oxide, poly(VBPO): polymer of VBPO, poly(VBPO-co-MMA): copolymer of VBPO and methyl methacrylate (MMA), MCQ: D,L-10-methacryloyloxy-camphorquinone, poly(MCQ): polymer of MCQ, poly(MCQ-co-BM): copolymer of MCQ and BM, poly(DMAEM): polymer of N,N-dimethylaminoethyl methacrylate poly(MCQ-co-BM-co-DMAEM): copolymer of MCQ, BM and DMAEM, HDDA: 1,6-hexanediol-diacylate, BA: *n*-butyl acrylate, TBB: tri-*n*-butyl borane, TBBQ: tri-*n*-butylborane oxide, poly(VBPO): polymer of VBPO, poly(VBPO-co-DAM): copolymer of VBPO and DAM, poly(TMBVPO-co-DAM): copolymer of TMBVPO and DAM

Methods: UV-VIS spectra: ultraviolet and visible spectra, DC: degree of conversion, λ_{max} : wavelength of maximum absorption, LED: light-emitting diode, QTH: quartz-tungsten halogen lamp, ESR: electron spin resonance, FT-IR: Fourier transform infrared spectra, ¹H NMR: proton nuclear magnetic resonance, ¹H-NMR-CIDNP: ¹H NMR-chemically induced dynamic nuclear polarization, DSC: differential scanning calorimeter, LB films: Langmuir–Blodgett films

water-soluble QTX in self-etching all-in-one adhesives on adhesion to polished dentin have been well investigated by Hayakawa *et al.*^{11–16} and Kikutake *et al.*^{17,18} and shown to be effective in improving the bond strength of composite resins to tooth substrates. In light of these encouraging results, a single-step hydrophobic adhesive which contained a water-soluble photoinitiator —sodium acylphosphine oxide (APONa)— and crown ether was synthesized, and its effect on adhesion to ground teeth was investigated¹⁹.

Further, to design a single-step self-etching adhesive, our recent study²⁰ was carried out to investigate the effect of a single-step, self-etching, HEMA-free adhesive —which contained a phosphonic acid monomer and a carboxylic acid monomer— on adhesion without the use of water-soluble photoinitiators.

The final chapter in this paper will discuss photoinitiating monomers and polymeric photoinitiators because they are now an attractive target for designing of biological injectable prepolymers, which are now widely used for biomedical applications such as bone cements and tooth filling materials.

Although number of light-curing dental adhesives

and resin composites are already commercially utilized, little review of the development of photoinitiators has been reported. Against this background of scarcity in published literature, our recent review paper²¹ discussed the effect of chemically-cured radical polymerization initiators on adhesion.

As for the present review paper, its focus is on our series of research and development studies on radical photopolymerization initiators which can potentially be used in the design of light-curing adhesives and resin composites. The aims of this review paper, therefore, were to discuss the following aspects:

1. Photochemistry of radical photopolymerization and photoinitiators in dentistry;
2. UV-VIS spectra, photopolymerization reactivities, and degrees of conversion of photoinitiators;
3. Effects of photoinitiators with light-curing units on photopolymerization;
4. Development of a novel camphorquinone derivative bearing an acylphosphine oxide group (CQ-APO);
5. Effect of water-soluble photoinitiator, QTX, in self-etching all-in-one adhesive on adhesion;
6. Effect of water-soluble photoinitiator, APO-Na,

with crown ether on adhesion;

7. Development of a new HEMA-free, self-etching adhesive without use of water-soluble photoinitiators;
8. Photoinitiating monomers and polymeric photoinitiators for biomedical applications.

Numerous materials and methods were used in this paper, and their abbreviations with full names are listed in Table 1.

PHOTOCHEMISTRY OF RADICAL PHOTOPOLYMERIZATION AND PHOTOINITIATORS IN DENTISTRY

Rapid progress of visible light-induced polymerization technology in dentistry

The photopolymerization technology is based on the use of photoreactive systems (which contain double bonds) suited to absorb a light irradiation of the appropriate wavelength and to produce primary radical species able to convert a multifunctional monomer into a cross-linked network¹⁾. The success of this technology hinges on the availability and action of appropriate photoinitiators, because the first step in the photopolymerization process is photoinitiation.

As for the photoinitiators, their success factors are linked to high absorptivity of the photoinitiator in the spectral region corresponding to the irradiating lamp emission, high efficacy in terms of both quantum yield for radical formation and high reactivity of the monomer formulation, good solubility in the curable medium, low odor and toxicity, and good storage stability¹⁾.

Considering the adverse health effects of ultraviolet light for oral soft tissues²⁾, visible-light induced radical polymerization has fast acceptance of photopolymerization technology in dentistry, and visible-light curing resin system has been rapidly progressing over the past three decades in dentistry rather than other radiation curing industry.

Moreover, compared to chemically cured and ultraviolet curing systems, the outstanding advantages of visible-light curing technology are its one-component nature, consistent handling characteristics, superior physical properties without the problem of microporosity and small voids, and improved adhesion. Coupled with the fast acceptance of photopolymerization technology in dentistry, visible light-induced radical polymerization has since become the widely applied process for bonding resins, resin composites, and composites for crown and bridge applications.

Invention of CQ/tertiary amine photoinitiator system

In 1971, Dart and Nemcek³⁾ (Imperial Chemical Industries Co. Ltd., UK) invented a visible light photoinitiator, α -diketone/tertiary amine, *i.e.*, D,L-camphorquinone (CQ)/*N,N*-dimethylaminoethyl methacrylate (DMAMA). This invention opened a new vista in the field of light-curing dental resins. By virtue of its outstanding performance for light-curing

dental resin composites and bonding resins, CQ/tertiary amine system has hitherto been recognized as an extremely valuable visible light initiator since its invention.

Another advantage of the α -diketone/tertiary amine system lies in its one-component packaging. This is because both α -diketone and tertiary amine can coexist in the dark, thereby enabling the formulations of composite pastes or bonding resins to be packaged as a single component in black or light-shielding containers.

Since α -diketone/tertiary amine system can coexist in dark, this photoinitiator system, differ from benzoyl peroxide (BPO)/aromatic tertiary amine, enables the formulation of composite pastes or bonding resins to a single pack component in black or light-shielding container.

Hydrogen abstraction initiating mechanism of CQ/amine photoinitiators

CQ displays its photoinitiating activity in combination with synergistic tertiary amines, hence the CQ/tertiary amine system is a so-called hydrogen abstraction (electron donating) type of photoinitiator. The underlying photoinitiation mechanism is that CQ [wavelength of maximum absorbance ($\lambda_{\max}$): 473 nm] absorbs visible rays to form an excited state (CQ*), and α -hydrogen of tertiary amine (reducing agent=hydrogen-donating agent) donates CQ* to form CQ-amine photoexcitation complex (=exciplex). After the complex decomposes to CQ-ketyl radicals (=hydryl $\cdot$ C-OH radicals) and aminyl $\cdot$ C-N radicals^{1,4)} (Fig. 1), the latter become the actual free radical species which initiate the crosslinking process whereas the former are mainly active in radical-radical recombination reactions¹⁾.

Although CQ/tertiary amine system offers many advantages, it must be pointed out that the tertiary

Fig. 1 Hydrogen abstraction photoinitiating mechanism of DL-camphorquinone (CQ) with tertiary amine. Tertiary amine (π acceptor) can react with an acidic group *i.e.*, phosphate or carboxyl group (π donor), in adhesion-promoting monomers to form undesirable quaternary ammonium salt⁴⁾.

Fig. 2 α -cleavage photoinitiation mechanism of acylphosphine oxide (APO) and bisacylphosphine oxide (BAPO)^{5). BAPO (a) undergoes initial α -cleavage from the triplet-excited state to yield radicals (b) and (c). Radical (c) is 2–6 times more reactive than (b)^{5).}}

amine (π acceptor) can react with an acidic group, *i.e.*, phosphoric acid, phosphonic acid, or carboxylic acid group (π donor) in adhesive monomers to form charge-transfer complexes (CT complexes)^{22,23) or undesirable quaternary ammonium salt⁴⁾ (Fig. 1). It was reported that the formation of quaternary ammonium salt resulted in increased time delay before light activation of the resin composite, hence ultimately resulting in degraded bond strength to dentin^{4).}}

α -cleavage photoinitiation mechanism of APO and BAPO

During the past several years, most efforts aimed at developing new photoinitiators have focused on developing new compounds that possess higher photoinitiation reactivity. To this end, acylphosphine oxide (APO) was invented by BASF Aktiengesellschaft, Germany and bisacylphosphine oxide (BAPO) by Ciba Specialty Chemicals Corp., NY, USA, and they were launched as commercial products.

Unlike CQ/amine photoinitiator system, APO and BAPO do not require tertiary amines. These photoinitiators undergo an α -cleavage type of photoinitiation mechanism (Norrish type I system)^{5,6)}, where 2,4,6-trimethylbenzoyl-diphenylphosphine oxide

(TMDPO) (=APO) undergoes rapid α -cleavage from a triplet excited state to yield the 2,4,6-trimethylbenzoyl radical $(\text{CH}_3)_3\text{Ph-C}^*(=\text{O})$ and diphenylphosphinoyl radical $(\text{Ph})_2\text{P}^*(=\text{O})$ ^{5,6,24–26)}. Both radicals are capable of initiating polymerization, but with different rate constants^{5,6)} (Fig. 2).

In an investigation by Sumiyoshi *et al.*⁶⁾ to elucidate the kinetics and mechanism of the photolysis of TMDPO in the presence of radical polymerizable monomers capable of undergoing α -cleavage-initiated photopolymerization, rather high rate constants (in $1 \text{ mol}^{-1}\text{s}^{-1}$) were found for the reactions of radicals with polymerizable olefinic monomers: 6.0×10^7 (methyl methacrylate), 6.0×10^7 (styrene). The quantum yield (ϕ) of radical formulation is ϕ (TMDPO)=0.5 to 0.7⁶⁾.

In another investigation by Kolczak *et al.*²⁵⁾, the reaction mechanisms of monoacyl- and bisacylphosphine oxide photoinitiators were studied using ^{31}P -, ^{13}C - and ^1H -NMR-CIDNP (chemically induced dynamic nuclear polarization) and electron spin resonance (ESR) spectroscopies. On the fate of the primary radicals, it was unambiguously shown by trapping experiments that BAPO photoinitiators generated four radicals in a stepwise process from a single precursor—a photochemical mechanism similar to that of APO photoinitiators²⁵⁾. In other words, active photopolymerization could be performed. For example, bis(2,4,6-trimethylbenzoyl)-phenylphosphine oxide (BTPPO)⁶⁾ (=BAPO) (a) underwent initial α -cleavage from the triplet excited state to form radicals $(\text{CH}_3)_3\text{Ph-C}^*(=\text{O})$ (b) and $(\text{CH}_3)_3\text{PhC}^*(=\text{O})-(\text{Ph})\text{P}^*(=\text{O})$ (c), as shown in Fig. 2. It was reported that (c) was 2–6 times more reactive than (b)^{5).}

UV-VIS SPECTRA, PHOTOPOLYMERIZATION REACTIVITIES, AND DEGREES OF CONVERSION OF PHOTOINITIATORS

UV-VIS spectra and photopolymerization times of APO and BAPO derivatives

The ultraviolet and visible (UV-VIS) spectra and photopolymerization reactivities of APO and BAPO derivatives were investigated in our previous study²⁷⁾. Figure 3 shows the UV-VIS spectra of 10 kinds of APO and BAPO derivatives as well as their corresponding structural formulas. Their full names are listed in Table 1.

According to their UV-VIS spectra, they possessed λ_{max} ranging between 365 and 416 nm. The λ_{max} of BDPO, NDPO, and IC 819 (=BAPO) were greater than 400 nm. As for the synthesized APO derivatives, there were slight differences in λ_{max} from the ultraviolet region to the visible light region although their structural formulas showed apparent differences. This could be caused by the $[>\text{P}(=\text{O})-\text{C}(=\text{O})-]$ moiety.

Figure 4 shows the method of measuring photopolymerization times using a differential scanning calorimeter (photo-DSC). Results showed that IC 819 (=BAPO), TMDPO (Lab), IC 1800, TMDPO (Com), and TMMPO demonstrated high photoinitiation reactivity

Fig. 3 The UV-VIS spectra of 10 kinds of APO and BAPO derivatives and their structural formulas. BDPO, TMMPO, TMDPO (Lab), PBDPO, TFBDOPO, DFDPO and NDPO were synthesized in our previous study²⁷⁾, whereas TMDPO (Com), IC 819, and IC 1800 were commercial reagents. Full names of all the photoinitiators are given in Table 1.

(Table 2). In sharp contrast, NDPO exhibited a long photopolymerization time (70.0 sec) with a broad photo-DSC peak—which might be caused by the naphthoyl group in the structure, while λ_{max} (401 nm) was slightly shifted to the visible light region²⁷⁾.

Degree of conversion achieved with APO, BAPO and CQ/tertiary amine

Degree of conversion (DC), which can be defined as the degree (%) of conversion of polymerizable monomers to

polymers, is a very important parameter used to measure polymerization performance. In the case of photopolymerization, DC is correlated with the physical properties of light-curing resins and is also influenced by multiple factors: the photopolymerization activity of photoinitiators and photosensitive resin monomers, and the wavelength and intensity of irradiation lamps. For these reasons, thorough and broad-ranging investigations on DC had to be carried out using several photoinitiators.

Fig. 4 Measurement of photopolymerization time (sec) with a differential scanning calorimeter (photo-DSC)²⁷⁾.

Fig. 5 Structural formulas of photoinitiators investigated by Arikawa *et al.*⁷⁾. Full names of CQ, PPD, TMDPO, and BCBPO are given in Table 1.

Table 2 UV-VIS spectra, physical appearance, melting points, and photopolymerization times of APO and BAPO derivatives investigated²⁷⁾

Photoinitiator	Classified as	Appearance	Melting point (K)	UV-VIS spectra ($\lambda_{\max}$, nm)	Photo-time (sec)
BDPO	APO	light yellow oily product	–	382, 398, 416	9.9 (0.5) ^a
TMMPO	APO	light yellow oily product	–	373	7.5 (0.4) ^b
TMDPO (Lab)	APO	white needle crystals	359–361	368, 382, 397	6.7 (0.5) ^{b,d}
TMDPO (Com)	APO	white powder	361–365	368, 382, 397	7.5 (0.8) ^b
PBDPO	APO	light yellow powder	473–478	368	inactivated
TFBDPO	APO	light yellow powder	–	380	inactivated
DFDPO	APO	light brown oily product	–	365, 379, 391	9.3 (0.5) ^a
NDPO	APO	light yellow powder	436–439	401	70.0 (5.5) ^c
IC 819	BAPO	light yellow powder	–	371, 400	5.9 (0.3) ^d
IC 1800	BAPO	light yellow powder	–	398	6.8 (0.5) ^{b,d}

Unfilled resins used: Bis-GMA/3G (60/40, wt%). Concentration of photoinitiators: 1.0 wt%. BDPO, TMMPO, TMDPO (Lab), PBDPO, TFBDPO, DFDPO, and NDPO were synthesized; TMDPO (Com), IC 819 and IC 1800 were commercial reagents. Photo-time: photopolymerization time (sec); $n=5$. Light intensity used for photo-DSC was 100 mWcm⁻¹. Groups from the same column that are identified with the same superscript letter are not significantly different ($p>0.05$). Full names of photoinitiators are given in Table 1.

Table 3 Degrees of conversion (%) of unfilled resins initiated by BAPO (IC1800) and CQ/EDAB initiator systems²⁷⁾

Unfilled resins (a)/(b)	BAPO (IC 1800) initiator		CQ/EDAB system	
	Group A	Group B	Group A'	Group B'
100/0	47.8 (6.7) ^a	47.4 (5.2) ^a	45.6 (2.8) ^a	46.1 (3.1) ^a
80/20	46.9 (6.5) ^a	49.2 (1.0) ^a	45.4 (2.3) ^a	46.2 (4.4) ^a
60/40	46.2 (4.6) ^a	51.2 (4.3) ^a	44.9 (4.2) ^a	47.5 (3.7) ^a
40/60	46.6 (5.5) ^a	45.2 (4.1) ^a	42.4 (4.4) ^a	45.7 (3.6) ^a
20/80	44.2 (6.5) ^a	44.4 (2.4) ^a	43.3 (5.7) ^a	43.0 (4.8) ^a
0/100	did not test	did not test	did not test	did not test
100% OH-monomer	did not test	did not test	did not test	did not test

$n=5$. Concentration of photoinitiators: BAPO (2.0 wt%), CQ/EDAB (0.5/1.0, wt%). OH-monomer: Group A and A': HEMA, Group B and B': GM. Group A and A': (a) Bis-GMA/3G (60/40, wt%)/(b) 6-MHPA/HEMA (50/50, wt%), Group B and B': (a) Bis-GMA/3G (60/40, wt%)/(b) 6-MHPA/GM (50/50, wt%). Groups from the same column that are identified with the same superscript letter are not significantly different ($p>0.05$). Full names of CQ, HEMA, GM, Bis-GMA, 3G, 6-MHPA, BAPO, IC 1800, CQ, and EDAB are given in Table 1.

In our recent study²⁷⁾ on the photopolymerization of APO-, BAPO- and CQ/tertiary amine-containing unfilled resins, DC (%) —as the degree of double bond conversion— was determined using Fourier transform infrared (FTIR) spectroscopy. As for the method reported in previous studies^{28,29)}, DC was obtained based on the subtraction of FTIR spectra measured before and after 30 seconds of light irradiation, using the residual percentage of polymerizable aliphatic double bond from 100%.

Table 3 presents the results of DC obtained. For the BAPO system, the DC values were 44.2(6.5)–51.2(4.3)%; for the CQ/ethyl *p*-*N,N*-dimethylaminobenzoate (EDAB) system, the DC values were 42.4(4.4)–47.5(3.7)%. Statistical analysis showed that there were no significant differences between the BAPO and CQ/EDAB systems among the different concentrations of 6-methacryloyloxyhexyl phosphonoacetate (6-MHPA)/HEMA and 6-MHPA/glycerol monomethacrylate (GM) in 2,2'-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (Bis-GMA)/triethyleneglycol dimethacrylate [TEGDMA (=3G)] resins ($p>0.05$).

Degree of conversion achieved with CQ/PPD system

Park *et al.*²⁹⁾ examined the synergistic effect of combining CQ with 1-phenyl-1,2-propanedione (PPD) (Fig. 5) as a new photoinitiator. PPD alone induced a DC that was not significantly different from that of CQ alone. When used in combination, CQ+PPD produced a DC which generally exceeded that produced by the same concentration of either used alone. Further, DC was increased by PPD but depressed by CQ, which was evidence that different mechanisms were involved. It should also be mentioned that PPD (λ_{max} : 410 nm) and CQ (λ_{max} : 473 nm) had different wavelength absorption ranges.

After 20 seconds of visible light irradiation with CQ/PPD system, DC obtained was 53%²⁹⁾. This was almost comparable with the DC values achieved with BAPO or CQ/EDAB in our study²⁷⁾, set against the backdrop that different photoinitiators and compositions were employed in both studies^{27,29)}.

EFFECTS OF PHOTOINITIATORS WITH LIGHT CURING UNITS ON PHOTOPOLYMERIZATION

DC (%) produced by four kinds of photoinitiators with four kinds of light curing units

Although APO (λ_{max} : 370 nm) exhibited excellent polymerization reactivity with violet LED lamp irradiation, it provided poor reactivity with dental blue LED lamp (420–510 nm, λ_{max} : 455 nm) because of its wavelength.

In a recent study by Arikawa *et al.*⁷⁾, the effects of photoinitiators with light curing units on the photopolymerization efficacy of unfilled light-curing resins were investigated. Figure 5 depicts the chemical structures of the four kinds of photoinitiators investigated —namely CQ, PPD, TMDPO, and bis(2,6-

dichlorobenzoyl)-(4-propylphenyl)phosphine oxide (BCBPO=BAPO). Each photoinitiator (1.5 wt%) was dissolved in a Bis-GMA (50 mol%) and TEGDMA (50 mol%) monomer mixture together with ethyl *p*-dimethylamino benzoate (EDAB) (0.2 wt%) as a reducing agent. Prepared unfilled resins were polymerized using a quartz-tungsten-halogen lamp (QTH), xenon plasma arc lamp (PAC), blue LED light curing unit, or a custom-made violet LED light unit.

Results showed that CQ- and TMDPO-containing resin could not be polymerized with the violet LED lamp and blue LED lamp respectively⁷⁾. PPD-, TMDPO-, and BAPO-containing resins (Bis-GMA/TEGDMA) polymerized with a violet LED light unit had approximately the same or higher degree of DC as compared with CQ-containing resin polymerized with a QTH lamp. On the overall, DC varied according to the combination of photoinitiator and curing light source. The ranges of DC values achieved with each light source were as follows: QTH: 64.8% (CQ)–75.5% (TMDPO); PAC: 51.1% (TMDPO)–58.1% (BAPO=IC 819); B-LED: 65.4 (PPD)–68.8% (CQ); V-LED: 61.4% (PPD)–77.5% (BAPO).

Photoinitiators activated with dental halogen, blue LED and Xenon lamps

Jandt *et al.*³⁰⁾ reported that the depth of cure and compressive strength of dental composites cured with a blue LED lamp were statistically equivalent to those cured with a conventional halogen lamp. This could be attributed to the advantage of a constant power output over the lifetime of the diodes, such that LED lamps are capable of achieving a clinically consistent quality of composite cure.

By means of ESR spectroscopy with a tapping method, Teshima *et al.*^{31,32)} quantified the primary radicals generated by irradiation by using phenyl-*tert*-butyl nitron (PBN) as a spin trapping agent. In their investigations^{31,32)}, two types of photoinitiator systems —CQ/*N,N*-dimethyl-*p*-toluidine (DMPT) and CQ/*N,N*-dimethylaminoethyl methacrylate (DMAEMA), and three types of light curing units— a blue LED unit [LUX-O-MAX (Panasonic Dental Co., Osaka, Japan)] and two conventional halogen units [Optilux 501 (Demetron/Kerr, Danbury, CT, USA) and XL 3000 (3M ESPE, St. Paul, MN, USA)] were used. Obtained peak wavelengths (nm) of the different light curing units were: LUX-O-MAX at 470 nm (430–525 nm), Optilux at 476 nm (375–530 nm), and XL3000 at 480 nm (400–530 nm).

Results showed that the CQ/DMPT photoinitiator system generated more radicals than the CQ/DMAEMA system^{31,32)}. It was suggested that DMAEMA molecules, which had methacryloyl group, produced DMAEMA-dimers or oligomers when radicals existed. On the influence of light curing units, the blue LED light of LUX-O-MAX generated 1.45–1.69 times as many radicals as the visible light of the halogen units. The latter result thus suggested that the LED unit, LUX-O-MAX, performed better than the conventional halogen

Fig. 6 Structural formulas of ketocoumarin compounds³⁴. CBEC: 3,3'-carbonylbis(7-diethylaminocoumarin), CBBC: 3,3'-carbonylbis(7-dibutylamino-coumarin).

Fig. 7 Structural formulas of novel acylphosphine oxide photoinitiators³⁵. TMBOPF: 9-(2,4,6-trimethylbenzoyl)-9-oxytho-9-phosphafuluorene, TOPF: 9-(*p*-toluy)-9-oxytho-9-phosphafuluorene.

light curing units with respect to the generation of primary radicals, *i.e.*, energy efficiency.

Recent patents^{33,34} claimed that the newly developed photoinitiator systems possessed good photoinitiation activities with dental halogen, blue LED and Xenon lamps. They are physically mixed, visible light curing initiators consisting of CQ, amine, and APO³³ or a system comprising APO or BAPO, accelerators, ketocoumarin compounds such as 3,3'-carbonylbis(7-diethylaminocoumarin) (CBEC) and 3,3'-carbonylbis(7-dibutylamino-coumarin) (CBBC) (Fig. 6), and with/without α -diketone³⁴.

Novel acylphosphine oxide photoinitiators: TMBOPF and TOPF

In a recent patent³⁵, novel acylphosphine oxide photoinitiators with a phosphol group were invented. They were namely, 9-(2,4,6-trimethylbenzoyl)-9-oxytho-9-phosphafuluorene (TMBOPF) and 9-(*p*-toluy)-9-oxytho-9-phosphafuluorene (TOPF) (Fig. 7). To achieve the TMBOPF structure, the diphenylphosphine oxide moiety [$>P(=O)-(\text{Ph})_2$] of APO was displaced with biphenyl phosphine oxide moiety [$>P(=O)-(\text{Ph}-\text{Ph})$] to form a five-member ring phosphol moiety.

Unlike conventional APOs, the novel TMBOPF and

TOPF photoinitiators exhibited good photopolymerization reactivity in both visible light and ultraviolet light ranges. In particular, TOPF-containing Bis-GMA-type resin exhibited good photopolymerization reactivity with a dental visible-light curing unit, and that its reactivity was comparable with that of BAPO (=IC 819) rather than that of APO.

On color stability, it was disclosed that the degree of yellow (DY) values of thick photo-cured coating films initiated by TMBOPF (DY: 1.9) and TOPF (DY: 2.3) with ultraviolet light irradiation were extremely reduced when compared against those of conventional APO (DY: 4.0) and BAPO (DY: 6.3)³⁵. With sunlight irradiation, the DY obtained with TOPF (DY: 5.7) was lower than that of BAPO (DY: 16.1). On formulation stability, the light-curing resin containing TMBOPF was more stable than that containing TOPF (our unpublished data).

DEVELOPMENT OF A NOVEL CAMPHORQUINONE DERIVATIVE BEARING AN ACYLPHOSPHINE OXIDE GROUP (CQ-APO)

Rationale behind the design of CQ-APO and its synthesis

Owing to its absorption wavelength, CQ has an inherently large *b* value in the CIELab color specification system, which is consequently manifested as a yellow tinge. On CQ derivatives, a Japanese patent³⁶ disclosed that 10 kinds of CQ derivatives, such as 2,3-dioxobicyclo[2.2.1]heptane with adhesive functional groups, possessed λ_{max} ranging between 459 and 472 nm. In other words, they could initiate visible light polymerization like CQ. Although these CQ derivatives were expected to be effective in promoting adhesion, concerns related to color tone remained to be investigated and addressed.

A recent patent³³ claimed that a physically mixed, visible light-curing initiator consisting of APO, CQ, and aliphatic amine exhibited excellent photopolymerization reactivity with both visible light and ultraviolet irradiators. However, this new invention³³ did not resolve the key CQ-related problems, namely short operation time and a high *b* value which was manifested as a tinge of yellow. In light of these unresolved problems, a research study⁸ was undertaken to develop a new photoinitiator which possessed reduced *b* value and high photopolymerization reactivity, but lengthened operation time—hence permitting a relaxed mode of therapeutic operation under ambient light.

To date, a photoinitiator having both α -diketone [$-C(=O)-C(=O)-$] and acylphosphine oxide [$>P(=O)-C(=O)-$] moieties bound intramolecularly is unknown. Our recent study⁸ thus newly designed and synthesized a novel 7,7-dimethyl-2,3-dioxobicyclo[2.2.1]heptane-1-carbonyl-diphenylphosphine oxide (DOHC-DPPO = CQ-APO).

Figure 8 is a schematic illustration of the synthesis of CQ-APO, which was synthesized by

Fig. 8 Schematic illustration of the synthesis of 7,7-dimethyl-2,3-dioxobicyclo[2.2.1]heptane-1-carbonyldiphenylphosphine oxide (CQ-APO)⁸⁾. Full names of KA, CQ-COOH, CQ-COCl, and MDPP are given in Table 1.

Fig. 9 Structural formulas of the photoinitiators or sensitizers and accelerators employed in the synthesis⁸⁾, except CQ-APO. Full names of CQ, TMDPO, EDAB, and Tin-Lau are given in Table 1.

Michaelis-Arbuzov reaction^{37,38)} between methoxydiphenylphosphine (MDPP) [CH₃O-P(Ph)₂] and 7,7-dimethyl-2,3-dioxobicyclo[2.2.1]heptane-1-carboxylic acid chloride (DOHCC=CQ-COCl). During this transformation, a trivalent phosphorus [P(III)] (=MDPP) was converted into a pentavalent phosphorus [P(V)] compound (=CQ-APO). As for CQ-COCl, it was synthesized by the reaction between 7,7-dimethyl-2,3-dioxobicyclo[2.2.1]heptane-1-carboxylic acid (DOHCA=CQ-COOH) and thionyl chloride. Figure 9 shows the structural formulas of the photoinitiators or sensitizers and accelerators employed in the synthesis⁸⁾, except CQ-APO.

UV-VIS spectral behaviors of CQ-APO, CQ, and TMDPO

Figures 10–12 show the UV-VIS spectral behaviors of CQ-APO, CQ, and TMDPO in dry toluene before and

Fig. 10 UV-VIS spectra of CQ-APO in dry toluene before and after light activation with a halogen lamp (light intensity: 650 mW/cm², wavelength region: 375–525 nm, λ_{max}=500 nm)⁸⁾.

Fig. 11 UV-VIS spectra of CQ in dry toluene before and after light activation with a halogen lamp (light intensity: 650 mW/cm², wavelength region: 375–525 nm, λ_{max}=500 nm)⁸⁾.

after light irradiation with a dental halogen lamp. On the UV-VIS spectrum before light irradiation, CQ and TMDPO (=APO) showed λ_{max}=472 nm and λ_{max}=382 nm respectively. It was noteworthy that CQ-APO showed continuous wide absorption from near-ultraviolet to visible region at 350–500 nm, whereby λ_{max}=372 nm was derived from the acylphosphine oxide group and λ_{max}=475 nm was derived from the α-diketone group.

On absorption coefficients, TMDPO exhibited a greater value than CQ-APO and which was considerably reduced to 19.0 M⁻¹cm⁻¹ (1/325) after light irradiation. As the latter value was approximately the same as that of CQ-APO, it could be said that the C-P

Fig. 12 UV-VIS spectra of TMDPO in dry toluene before and after light activation with a halogen lamp (light intensity: 650 mW/cm², wavelength region: 375–525 nm, $\lambda_{\max}$ =500 nm)⁸⁾.

cleavage of $[-C(=O)-P(=O)<]$ bond around 380 nm was generated in both CQ-APO and TMDPO after light irradiation, *via* α -cleavage type of photoinitiation mechanism (Norrish type I system)^{5,6)}. Unlike α -cleavage type, as for CQ, slow hydrogen abstraction from the toluene solvent did not lead to considerable reduction in absorption coefficient.

Relationship between color tone and spectral absorption

It was surprisingly found that CQ-APO—in which CQ and APO groups were bound intramolecularly—exhibited excellent color tone stability with a small *b* value of 4.0 (Table 4). In contrast, conventional CQ alone and physically mixed CQ/TMDPO exhibited large *b* values of 84.0 and 87.8 respectively. Therefore, it was apparent that CQ-APO provided considerable improvement in color tone⁸⁾.

On the relationship between color tone and absorption spectrum, a substance which absorbs light in the visible light region (approx. 400–800 nm) reflects a color whereas a substance which absorbs light in the near-ultraviolet region does not reflect any color. On this premise, CQ appeared yellow whereas TMDPO had a colorless appearance. For CQ-APO, a colorless appearance like that of TMDPO was presented when maximum absorption occurred at $\lambda_{\max}$ =372 nm in the near-ultraviolet region. However, for absorption in the visible light region at $\lambda_{\max}$ =475 nm, a color was reflected.

When the absorption coefficient of CQ-APO was compared with that of CQ *circa* 470 nm, the former was about 1/5 that of the latter (Figs. 10 and 11). Owing to this considerable difference in absorption coefficient values, CQ-APO appeared as a very pale yellow crystal as compared to the intense yellow appearance of CQ. Based on these observations, it was

Fig. 13 Schematic illustration of a plausible photoinitiation mechanism of CQ-APO⁸⁾. CQ-APO could undergo both α -cleavage initiation to form the $[CQ-(O\equiv)C\cdot]$ and $[P(=O)(Ph)_2]^{5,6)}$ radicals as well as hydrogen abstraction initiation to form CQ-APO ketyl radical and free radicals *via* the formation of CQ*-APO-amine exciplex. Moreover, the CQ-APO ketyl radical may undergo C-P cleavage to form free radicals⁸⁾.

Fig. 14 Stereochemical structures of CQ-APO (left) and D,L-camphorquinone (right) from the views of α -diketone group indicated by arrows a and b by α -diketone group⁸⁾. Atoms: blue balls=H, black balls=C, red balls=O, pink balls=P. In a stable structure in potential energy, α -diketone group of CQ-APO had a slightly strained structure while that of CQ had a plane structure⁸⁾.

presumed that CQ-APO possessed a *b* color parameter of very small value.

Plausible photoinitiation mechanism of novel CQ-APO

CQ-APO possessed both APO moiety ($\lambda_{\max}=372$ nm) and CQ moiety ($\lambda_{\max}=475$ nm) in its chemical structure. Therefore, it was plausible to suggest that upon light activation, both α -cleavage type and hydrogen abstraction type of initiation mechanisms were triggered within CQ-APO.

Figure 13 is a schematic illustration of the plausible photoinitiation mechanism of CQ-APO. It was suggested that CQ-APO underwent rapid α -cleavage of the $[-C(=O)-P(=O)<]$ bond from a triplet state to afford the $[CQ-(O)=C\cdot]$ and diphenylphosphinoyl

$[P(=O)(Ph)_2\cdot]$ radicals^{5,6}, like the photoinitiation mechanism of acylphosphine oxide^{25,27}. In the case of CQ-APO with an electron donating agent such as a tertiary amine, it is also noteworthy that after α -diketone $[-C(=O)-C(=O)-]$ of CQ-APO absorbed the energy of visible rays to convert into an excited state (CQ*-APO), α -hydrogen of tertiary amine would donate CQ*-APO to form CQ*-APO-amine exciplex (excited state complex). The latter might be subsequently decomposed to CQ-APO ketyl radical and free radicals derived from tertiary amines, like the photoinitiation mechanism of camphorquinone²⁷. Moreover, unlike an inactivated CQ-ketyl radical, the CQ-APO ketyl radical might undergo C-P cleavage to form free radicals (Fig. 13). To gain more insight into the kinetics of the

Table 4 Compositions and photopolymerization of experimental, visible light-curing, unfilled resins^{§)}

Ingredients (parts by weight)	UR-1	UR-2	UR-3	UR-4	UR-5	UR-6	UR-7
CQ-APO	2.0	–	–	–	2.0	–	–
CQ	–	2.0	–	2.0	–	2.0	2.0
TMDPO	–	–	1.0	1.0	–	–	1.0
EDAB	–	–	–	–	1.0	1.0	1.0
Bis-GMA	60.0	60.0	60.0	60.0	60.0	60.0	60.0
TEGDMA	40.0	40.0	40.0	40.0	40.0	40.0	40.0
Reactivity (Hal/30 sec)	A	C	A	A	A	A	A
Reactivity (LED/10 sec)	B	C	D	C	A	A	A
Photo-time (sec)	NT	NT	NT	NT	9.6 (0.5) ^a	10.9 (0.7) ^a	8.5 (0.6) ^a
Operation time (sec)	NT	NT	NT	NT	50.0 (2.5) ^a	5.0 (1.0) ^b	5.0 (0.5) ^b
<i>b</i> value	4.0	84.0	6.1	87.8	6.4	83.1	88.8

Scoring of photopolymerization reactivity, where A: extremely high, B: high, C: low, D: no reactivity. Photo-time: photopolymerization time, NT: not tested, *b* value of color tone: measured immediately after photopolymerization. Groups from the same column that are identified with the same superscript letter are not significantly different ($p>0.05$). Full names of CQ-APO, CQ, TMDPO, EDAB, Bis-GMA, and TEGDMA are given in Table 1.

Table 5 Compositions and photopolymerization of experimental, visible light-curing resin composites^{§)}

Ingredients (parts by weight)	CR-1	CR-2	CR-3	CR-4	CR-5
CQ-APO	2.5	2.5	2.5	2.5	2.5
Tin-Lau	1.5	1.5	1.5	1.5	1.5
TMDPO	–	0.5	1.0	–	0.5
UDMA	60.0	60.0	60.0	–	–
Bis-GMA	–	–	–	60.0	60.0
TMPT	40.0	40.0	40.0	40.0	40.0
4-AET	0.5	0.5	0.5	0.5	0.5
Silica filler	271.4	271.4	271.4	271.4	271.4
Fine particle filler	8.4	8.4	8.4	8.4	8.4
Photo-time (sec)	14.4 (1.5) ^a	9.6 (0.8) ^b	10.5 (0.8) ^b	10.8 (0.5) ^b	8.8 (0.5) ^b
Operation time (sec)	150.0 (15) ^a	150.0 (15) ^a	140.0 (10) ^a	140.0 (15) ^a	130.0 (15) ^a
Flexural strength (MPa)	114.3 (10.2) ^a	122.1 (11.3) ^a	113.5 (12.2) ^a	124.5 (12.2) ^a	133.8 (13.5) ^a
Flexural modulus (GPa)	10.2 (1.3) ^a	11.6 (1.5) ^a	12.3 (1.6) ^a	11.8 (1.8) ^a	13.5 (2.1) ^a
<i>b</i> value	16.7	18.3	18.7	17.5	18.6

Photo-time: photopolymerization time, *b* value of color tone: measured immediately after photopolymerization. Groups from the same column that are identified with the same superscript letter are not significantly different ($p>0.05$). Full names of Tin-Lau, UDMA, TMPT, CQ-APO, TMDPO and Bis-GMA are given in Table 1.

photoinitiation mechanism of CQ-APO, it is expedient to perform quantum yield measurement by ESR spectroscopy.

Relationship between color tone and molecular structure

On the relationship between color tone and molecular structure for CQ-APO and CQ, Fig. 14 illustrates their stereochemical structures from the views of the α -diketone group [$-C(=O)-C(=O)-$] indicated by arrows a and b⁸⁾. In a stable structure in potential energy, the α -diketone group of CQ was given a plane structure (Fig. 14b). However, the α -diketone group of CQ-APO had a slightly strained structure (Fig. 14a). It was thought that the slightly strained structure of α -diketone group in CQ-APO might be instrumental in yielding a small *b* value for the yellow shade.

Photopolymerization reactivity, photopolymerization time, operation time, flexural strength and flexural modulus

Physically mixed photoinitiators, namely CQ-APO/Tin-Lau and CQ-APO/Tin-Lau/TMDPO which acted synergistically, exhibited short photopolymerization time and a longer operation time (Table 5). In particular, CR-5—which contained the novel ternary photoinitiator, CQ-APO/Tin-Lau/TMDPO—exhibited the highest flexural strength (133.8 MPa) and flexural modulus (13.5 GPa) (Table 5).

Due to the presence of CQ-APO, CQ-APO/Tin-Lau and CQ-APO/Tin-Lau/TMDPO not only underwent α -cleavage type of photoinitiation, but also hydrogen abstraction type of photoinitiation with electron donating agents (*i.e.*, tertiary amine or dibutyltin dilaurate), to generate several kinds of free radicals. Consequently, it was achieved an invention termed as “Camphorquinone derivative having acylphosphine oxide group, and containing the same, photopolymerization catalyst and photo/chemical polymerization catalyst, and containing these, hardenable composition”³⁹⁾.

As aliphatic acyldiphenylphosphine oxides are unstable in hydrolytic conditions⁴⁰⁾, CQ-APO was formulated with Bis-GMA as a base resin in our research study⁸⁾, whereby Bis-GMA is a hydrophobic radical polymerizable monomer. Further, CQ-APO without benzoyl moiety would be a more favorable candidate in improving biocompatibility than TMDPO which releases 2,4,6-trimethylbenzoyl radicals.

EFFECT OF WATER-SOLUBLE PHOTOINITIATOR, QTX, IN SELF-ETCHING ALL-IN-ONE ADHESIVE ON ADHESION

Invention of a water-soluble photoinitiator QTX for water-based dental adhesives

Masuhara *et al.*^{9,10)} found that water-reactive TBB initiator enabled hydrophobic MMA to adhere strongly to moist adherends while MMA monomer has 21 vol% shrinkage⁴¹⁾. In light of this finding, several research efforts have focused on designing and developing water-

Fig. 15 Chemical structures of materials used in the studies^{12–15)} by Hayakawa *et al.* Full names of QTX, CQ, EDAB, PIDAA, DMAEM, BSNa, MTYA, 10-MDP, HEMA, BPE, GMR, and GAM are given in Table 1.

soluble photoinitiators with an initiation performance like TBB initiator^{9,10)}.

In 1986, Davis *et al.*⁴²⁾ synthesized a series of novel water-soluble thioxanthone photoinitiators. Following this development⁴²⁾, water-based self-etching adhesives containing water-soluble, visible light photoinitiators^{11–18)} have been extensively investigated and reported—in particular, 2-hydroxy-3-(3,4-dimethyl-9-oxo-9H-thioxanthen-2-yloxy)-N,N,N-trimethyl-1-propanaminium chloride (QTX) ($\lambda_{\text{max}} = \text{circa } 500 \text{ nm}$). Hayakawa *et al.*^{11–16)} reported that water-soluble QTX in self-etching adhesives provided efficient adhesion to polished dentin, and their research work culminated in the invention of a water-based photocurable adhesive composition comprising QTX¹⁴⁾.

Effect of water-soluble photoinitiator QTX with adhesive monomers on adhesion

Figure 15 shows the chemical structures of QTX, amines, and monomers employed in the series of QTX studies by Hayakawa *et al.*^{12–15)}. In their early study¹²⁾, QTX was incorporated in aqueous bonding resin comprising methacryloyl tyrosine amide (MTYA) and glutaraldehyde (GA), and a tensile bond strength of 12 MPa was obtained after 5 minutes of application on polished dentin.

In their subsequent studies, Hayakawa *et al.*^{13–15)}

Table 6 Effect of photoinitiator addition to self-etching, 30 M primer on adhesion of resin composite to dentin and enamel¹³⁾

Photoinitiator (concentration: wt%)	Tensile bond strength (mean±SD, MPa)	
	Dentin	Enamel
without photoinitiator	7.8 (3.0) ^a	13.7 (4.9) ^ω
CQ (0.5)	7.3 (3.8) ^a	13.5 (5.3) ^ω
CQ (1.0)	6.0 (3.2) ^a	14.6 (5.1) ^ω
CQ (3.0)	7.3 (3.8) ^a	11.4 (4.9) ^ω
QTX (0.3)	12.8 (5.4) ^b	12.8 (5.3) ^ω
QTX (0.5)	11.8 (8.4) ^b	12.2 (4.6) ^ω
QTX (3.0)	7.2 (3.1) ^a	14.2 (5.2) ^ω
QTX (5.0)	5.6 (3.5) ^a	16.3 (6.3) ^ω

$n=10$ for each treatment. 30 M primer: 30 wt% 10-MDP/35 wt% HEMA/35 wt% water (pH: 1.02), SD: standard deviation. Groups from the same column that are identified with the same superscript letter (a, b, or ω) are not significantly different ($p>0.05$). Full names of QTX, CQ and 10-MDP are given in Table 1.

Table 7 Compositions of self-etching primer adhesives containing QTX¹⁵⁾

Abbreviation of adhesives	10-MDP	HEMA	Water-soluble dimethacrylates			QTX	Amines	
			BPE	GMR	GAM		EDAB	PIDAA
BPE	5	35	30	—	—	3	0.5	—
GMR	5	35	—	30	—	3	0.5	—
GAM	5	35	—	—	30	3	0.5	—
GMR-PIDAA	5	35	—	30	—	—	—	0.5

Full names of 10-MDP, HEMA, BPE, GMR, GAM, QTX, EDAB, and PIDAA are given in Table 1.

Table 8 Tensile bond strengths of resin composite to bovine dentin and enamel with different self-etching QTX-containing primer adhesives (BPE, GMR, GAM, and GMR-PIDAA)¹⁵⁾

Self-etching primer adhesive	Tensile bond strength (mean±SD, MPa)	
	Dentin	Enamel
BPE	12.3 (5.6) ^δ	14.3 (2.4) ^{ω, δ}
GMR	13.2 (3.3) ^{a, δ}	17.2 (6.1) ^{ω, δ}
GAM	11.3 (3.3) ^{a, δ}	16.1 (5.8) ^{ω, δ}
GMR-PIDAA	19.8 (5.2) ^{b, δ}	20.8 (6.4) ^{ω, δ}

$n=10$ for each treatment, SD: standard deviation. Groups from the same column that are identified with the same superscript letters (a, b, or ω) are not significantly different ($p>0.05$). Letter δ indicates mean values that are not significantly different between dentin and enamel for the same self-etching primer adhesive treatment ($p>0.05$). Full names of QTX, BPE, GMR and GAM are given in Table 1.

further investigated the effect of the dual presence of QTX and acidic adhesive monomers in self-etching primers on adhesion to smear layer-covered polished dentin. Self-etching primers containing 30 wt% 10-methacryloyloxydecyl dihydrogen phosphate (10-MDP), 35 wt% HEMA, and 35 wt% water (30 M; pH value=1.02) were thus prepared, containing either 0.5–3.0 wt% CQ or 0.3–5.0 wt% QTX¹³⁾.

Table 6 presents the tensile bond strengths of resin composite to polished bovine dentin and enamel using the self-etching adhesives¹³⁾. The addition of hydrophobic CQ to 30 M self-etching primer did not increase the bond strength to dentin. However, the addition of water-soluble QTX at 0.3 wt% and 0.5 wt% significantly ($p<0.05$) increased the dentin bond strength to 12.8 MPa and 11.8 MPa respectively. On bond strength to enamel, neither the addition of CQ

nor QTX to the self-etching primer (30 M) brought about any significant increase.

Effects of water-soluble dimethacrylates and amines in QTX-containing all-in-one adhesive on adhesion

According to the formulations listed in Table 7¹⁵⁾, experimental all-in-one adhesives were prepared using different combinations of glycerol dimethacrylate (GMR) or glycerol methacrylate acrylate (GAM), ethyl *p*-(*N,N*-dimethylamino)benzoate (EDAB), *N*-phenyliminodiacetic acid (PIDAA), 2,2-bis(4-methacryloyloxy polyethoxyphenyl)propane (BPE), 10-MDP, HEMA, and QTX.

Table 8 presents the tensile bond strengths of resin composite to tooth substrates using these experimental QTX-containing adhesives. Differences in water-soluble dimethacrylate monomers did not produce any

significant differences in tensile bond strength to dentin or enamel. The use of PIDAA instead of EDAB showed significantly higher bond strength to dentin and enamel. In particular, the tensile bond strength of GMR-PIDAA to dentin (19.8 ± 5.2 MPa) was significantly higher than that of GMR to dentin (13.2 ± 3.3 MPa) ($p < 0.05$). For enamel adhesion, there were no significant differences in tensile bond strength between GMR-PIDAA and GMR ($p > 0.05$), but the highest bond strength of 20.8 ± 6.4 MPa to polished enamel was obtained with GMR-PIDAA¹⁵. Therefore, the combination of PIDAA and QTX was effective in improving the bond strength of resin composite to dentin and enamel in an all-in-one bonding system, and water-soluble GMR and GMA were useful as a component of the original primer adhesive¹⁶.

On the bonding mechanism to dentin, it was suggested that QTX diffused into the moist dentin substrate and initiated an *in situ* photopolymerization, where the acidic adhesive monomers interacted with the polished dentin substrate to form stronger adhesion as compared to the hydrophobic CQ/tertiary amine system^{13–15}.

Since tertiary amines (*i.e.*, PIDAA and EDAB) accelerated the photopolymerization process^{15,18}, it was probable that QTX performed a hydrogen abstraction initiation mechanism similar to that of CQ/tertiary amine system. It was thus anticipated that tertiary amines (π acceptor) could react with acidic groups (π donor) (*i.e.*, phosphoric acid, phosphonic acid, and carboxyl groups) of adhesive monomers to form

undesirable quaternary ammonium salts⁴) or charge-transfer complexes (CT complexes) with adverse effects^{22,23}) on initiation reactivity and adhesion.

EFFECT OF A WATER-SOLUBLE PHOTOINITIATOR, APO-NA, WITH CROWN ETHER ON ADHESION

Design of hydrophobic water-free adhesives comprising water-soluble APO-Na with crown ether

In previous studies^{11–18}) on water-soluble photoinitiators, the focus was almost exclusively on QTX in water-based self-etching adhesives. In our research study, the focus was shifted to a water-soluble photoinitiator, sodium acylphosphine oxide (APO-Na), in water-free hydrophobic adhesives¹⁹.

The behavior of water-soluble photoinitiators with crown ethers in dental adhesives was an unknown. Our recent study¹⁹) thus aimed to investigate the effect of APO-Na with crown ether in a hydrophobic adhesive on adhesion to teeth.

APO-Na was synthesized by the reaction between sodium iodide (NaI) and 2,4,6-trimethylbenzoyl-methoxy-phenylphosphine oxide (TMMPO), which was synthesized by Michaelis–Arbuzov reaction^{37,38}) between 2,4,6-trimethylbenzoyl chloride (TMC) and dimethoxyphenyl phosphine (DMPP). To dissolve APO-Na as a sodium salt in hydrophobic water-free resins, crown ethers known as clathrate or inclusion compounds were considered. Figure 16 shows the structural formulas of the materials used in the study¹⁹.

Fig. 16 Structural formulas of the materials employed in the study¹⁸) by Ikemura *et al.* Full names of TMPO-Na (=APO-Na), TMDPO (=APO), 6-MHPA, TEGDMA, 4-MET, and Bis-GMA are given in Table 1.

Fig. 17 A photograph of two unfilled resins with (left: Resin A) and without (right: Resin B) 18-crown-6¹⁹). It is apparent that APO-Na powder was dissolved in hydrophobic Bis-GMA/TEGDMA resin in the presence of crown ether to form a clear liquid (Resin A). On the contrary, Resin B without crown ether appears turbid because the white powder of APO-Na was not dissolved in hydrophobic resin.

Table 9 Effect of the concentration of crown ether in experimental, one-bottle, single-step bonding resins on shear bond strength (SBS) to unetched ground enamel and dentin (Method A)¹⁹⁾

6-MHPA /4-MET (wt%)	Bis-GMA/ TEGDMA (60/40) (wt%)	APO-Na (wt%)	CE-6 (wt%)	Acetone (wt%)	SBS to Enamel [MPa (SD)]	SBS to Dentin [MPa (SD)]
15.0/20.0	35.0	0.50	–	29.50	2.3 (1.2) ^a	2.5 (0.8) ^a
15.0/20.0	35.0	0.50	0.25	29.25	11.3 (3.4) ^b	12.8 (4.2) ^b
15.0/20.0	35.0	0.50	0.50	29.00	13.6 (3.3) ^b	14.1 (3.6) ^b
15.0/20.0	35.0	0.50	1.00	28.50	8.2 (3.8) ^b	10.5 (4.7) ^b
15.0/20.0	35.0	APO: 0.50	–	29.50	7.4 (2.4) ^b	5.3 (2.6) ^c

$n=10$, SD: standard deviation. Method A: One-bottle single-step adhesive, where bonding resin was applied to ground teeth. Groups from the same column that are identified with the same superscript letter are not significantly different ($p>0.05$). Full names of 6-MHPA, 4-MET, Bis-GMA, TEGDMA, APO-Na (=TMPO-Na), and CE-6 are given in Table 1.

Table 10 Effect of the concentration of acidic adhesive monomers (6-MHPA and 4-MET) in experimental, two-bottle, single-step bonding resins on shear bond strength (SBS) to unetched ground enamel and dentin (Method B)¹⁹⁾

6-MHPA (wt%)	4-MET (wt%)	Bis-GMA/ TEGDMA (60/40) (wt%)	APO-Na (wt%)	CE-6 (wt%)	Acetone (wt%)	SBS to Enamel [MPa (SD)]	SBS to Dentin [MPa (SD)]
0	0	70.0	0.5	0.5	29.0	2.2 (0.8) ^a	1.1 (1.5) ^b
12.0	16.0	42.0	0.5	0.5	29.0	17.1 (3.8) ^b	15.8 (4.3) ^b
15.0	20.0	35.0	0.5	0.5	29.0	17.9 (3.5) ^b	14.1 (3.8) ^b
18.0	24.0	28.0	0.5	0.5	29.0	16.5 (3.9) ^b	15.5 (4.6) ^b
21.0	28.0	21.0	0.5	0.5	29.0	16.3 (4.2) ^b	20.2 (4.7) ^b

$n=10$, SD: standard deviation. Method B: Two-bottle single-step adhesive, where bonding resin was mixed with PTS solution (p -TSNa/acetone/water=3.0/27/70 wt%) and applied to ground teeth. Groups from the same column that are identified with the same superscript letter are not significantly different ($p>0.05$). Full names of 6-MHPA, 4-MET, APO-Na, CE-6, Bis-GMA, and TEGDMA are given in Table 1.

Ionophor effect of crown ethers and optimal concentration of APO-Na and crown ether

An outstanding characteristic of crown ethers is their ability to embed inorganic cations (*i.e.*, APO-Na) or amino acids (in NH_3^+) in their cavity, hence they are known for their ability to strongly solvate cations. This is the so-called ionophore effect⁴³⁾ shown in Fig. 17, which enabled water-soluble APO-Na to dissolve in hydrophobic adhesive solutions in the presence of crown ether.

Experimental water-free adhesives comprising APO-Na, CE, Bis-GMA, 6-methacryloyloxyhexyl phosphonoacetate (6-MHPA), and 4-methacryloyloxyethyltrimellitic acid (4-MET) were prepared. Their compositions are shown in Tables 9 and 10. Shear bond strengths of resin composites with these adhesives to unetched ground teeth were measured at a crosshead speed of 1.0 mm/min, and the data were analyzed by ANOVA.

Table 9 presents the effects of the concentration of 18-crown-6-ether (CE-6) with APO-Na in one-bottle bonding resins on adhesion to unetched-ground enamel and dentin. One-bottle bonding resin was directly applied to ground enamel or dentin as a one-bottle, single-step, bonding resin (Method A). Based on the shear bond strength results shown in Table 9, the optimal concentration was determined to be 0.5 wt%

for both APO-Na and CE-6, at which the highest bond strength values were obtained for ground enamel (13.6 ± 3.3 MPa) and ground dentin (14.1 ± 3.6 MPa).

Effect of adhesive monomers in APO-Na-containing adhesives on adhesion and bonding mechanism

Table 10 presents the effects of the concentration of acidic adhesive monomers (6-MHPA and 4-MET) with APO-Na and CE-6 in the bonding resins on adhesion to unetched ground enamel and dentin. PTS-solution [a mixture of p -TSNa/acetone/water=3.0/27/70 (wt%)] was employed for Method B (two-bottle, single-step).

It was apparent that the shear bond strengths of 6-MHPA- and 4-MET-containing bonding resins to both ground enamel and dentin were significantly higher than that without these adhesive monomers ($p<0.05$). For bonding to enamel, highest shear bond (17.9 ± 3.5 MPa) was achieved with the adhesive containing 15.0 wt% 6-MHPA/20.0 wt% 4-MET; for bonding to dentin, highest shear bond strength (20.2 ± 4.7 MPa) was achieved with the adhesive containing 21.0 wt% 6-MHPA/28.0 wt% 4-MET. These results confirmed that water aptly controlled and regulated the bonding function of adhesive monomers to the tooth substrates. These findings eventually culminated in the invention termed as “A curable composition comprising clathrate compounds”⁴⁴⁾.

6-MHPA and 4-MET are known as an amphiphilic molecules that have both hydrophilic and hydrophobic parts. On the underlying bonding mechanism to the tooth substrates, it was hypothesized based on the theory of Langmuir-Blodgett (LB) films⁴⁵) that the ionized hydrophilic parts [i.e., $-P(=O)(O^-)_2$, $-COO^-$] interacted with hydroxyapatite in the tooth substrates, wherein ionized APO-Na ($-O^-Na^+$) then initiated *in situ* photopolymerization at the resin-tooth interface to improve adhesion.

Stability of APO-Na and biological safety of crown ethers

On photoinitiator stability, APO and BAPO derivatives are generally prone to undergoing solvolytic cleavage of the C-P bond [$>P(C=O)-(C=O)-$] in the presence of nucleophilic compounds, such as water. However, it has been shown that the solvolytic stability of acylphosphine oxides could be greatly enhanced by the substituent effect of stereochemistry, where the presence of methyl group in the ortho positions enabled the carbonyl group to be shielded from nucleophilic attack⁴⁰.

For this reason, commercially utilized APO and BAPO have trimethylbenzoyl moiety to improve their solvolytic stability⁵) and render them more stable in hydrophobic resins such as Bis-GMA resin. Similarly, due to the presence of trimethylbenzoyl moiety in the structure, TMPO-Na (APO-Na) was stable in Bis-GMA/TEGDMA resins.

Although APO-Na with crown ether had favorably contributed to efficient adhesion with the tooth substrates, the toxicity of crown ethers must also be duly highlighted at this juncture. On the toxicity of crown ethers, the acute LD₅₀ (lethal dose, 50 percent kill) values in mice of 12-crown-4, 15-crown-5, and 18-crown-6 are 3,150 mg/kg, 1,020 mg/kg, and 7,100 mg/kg respectively⁴⁶.

DEVELOPMENT OF A NEW HEMA-FREE, SELF-ETCHING ADHESIVE WITHOUT USE OF WATER-SOLUBLE PHOTOINITIATORS

Rationale for developing HEMA-free bonding resins without the use of water-soluble photoinitiators

In our recent study¹⁹) on the effect of APO-Na on adhesion, the experimental bonding resins—unlike conventional self-etching adhesives—contained neither water nor HEMA. Although APO-Na with crown ether markedly improved the bond strength of hydrophobic adhesives to ground enamel and dentin, there remain some major biosafety issues of crown ethers to contend with.

Nonetheless, based on the encouraging results of HEMA-free, APO-Na-containing adhesives toward adhesion¹⁹), our next research target was to develop a HEMA-free, self-etching adhesive without the use of water-soluble photoinitiators.

Inherent disadvantages of HEMA for single-bottle adhesives

A number of compromises have to be made when self-etching adhesives are simplified into single-bottle formulations⁴⁷) that usually contain acidic adhesive monomers, together with both water and water-soluble monomers, such as HEMA.

HEMA has several inherent disadvantages. It retains water within the adhesive layer and causes the mechanical strength to be adversely affected⁴⁸); 70% of HEMA could be hydrolyzed in 37°C acidic solutions (pH 1.0) within a week⁴⁹); it causes delayed allergic reactions in sensitized persons⁵⁰). Since HEMA provides low photopolymerization reactivity²⁷), it also meant that the bonding layer containing HEMA would produce low physical properties with high water absorption characteristic, thereby resulting in poor bonding durability to teeth. Conversely, it was anticipated that a HEMA-free adhesive would produce good physical properties with good bonding durability.

Development of HEMA-free single-bottle bonding resin

In our recent study²⁰), the effect of experimental HEMA-free, single-step, self-etching adhesives containing conventional CQ/tertiary amine initiator on adhesion was further investigated. It was found that the experimental HEMA-free self-etching adhesives adhered strongly to ground enamel and dentin, and an invention entitled “A pH-controlled adhesive composition”⁵¹) was achieved.

Recently, a new one-bottle single-step, HEMA-free, self-etching bonding resin BeautiBond (Shofu Inc., Kyoto, Japan) was developed and introduced to the dental market (2008). As a seventh-generation adhesive, BeautiBond exhibits the advantages of being fast and easy to use, with better adhesion to both enamel and dentin in a single step⁵²).

PHOTOINITIATING MONOMERS AND POLYMERIC PHOTOINITIATORS FOR BIOMEDICAL APPLICATION

Photoinitiators for biomedical applications

Currently, photoinitiating monomers and polymeric photoinitiators are widely used for biomedical applications such as bone cements and tooth filling materials. *In vivo* polymerization of injectable prepolymer liquids provides the possibility of forming polymers in complex shapes⁴⁰). This means that implantation can be performed through small holes and is therefore less invasive than conventional surgical techniques⁴⁰).

During photopolymerization, insufficient reactivity of photoinitiators will cause a substantial amount of unreacted and less reacted photoinitiator fragments to remain and subsequently migrate out of the photopolymerized material⁴⁰). To overcome this problem, it is well investigated so-called polymeric photoinitiators which bear photosensitive moieties in the side chains of their polymer chemical structures,

thereby bestowing their macromolecular structures with important reactivity-related advantages.

Synthesis of visible light photoinitiating monomer containing anthraquinone

Recently, several photoinitiating monomers defined as compounds bearing photoinitiating moiety and radical polymerizable group intramolecularly were developed. They are radical polymerizable photoinitiators, and they act as self-crosslinking species as well as photoinitiators.

Notably, Takeuchi and Mizuta⁵³⁾ invented a photocurable resin composition containing an anthraquinone derivative, which comprised a polymerizable moiety intramolecularly, as a photoinitiating monomer. One of the derivatives (HTAQ-MEI) was synthesized by the reaction between 2-(2-hydroxyethylthio)-9,10-anthraquinone (HTAQ) and 2-methacryloyloxyethyl isocyanate (MEI) (Fig. 18). It was disclosed that HTAQ-MEI exhibited excellent reactivity under both ultraviolet and visible light irradiation and that occurrences of outgassing from hardened materials during photopolymerization were minimal.

Synthesis of visible light-photoinitiated vinyl-functional acylphosphine oxides

Although 2,4,6-trimethylbenzoyl group contributed to the photoinitiator stability of TMDPO initiator, the benzoyl radicals generated as a result of the α -cleavage of TMDPO posed a biological hazard⁴⁰⁾ in biomedical and dental applications.

To develop photoinitiating monomers for biomedical applications, de Groot *et al.*⁴⁰⁾ synthesized three kinds of vinyl-functional acylphosphine oxides, as depicted in Fig. 19: 4-vinylbenzoyl diphenylphosphine oxide (VBPO), 2,6-dimethyl-4-vinylbenzoyl-diphenylphosphine oxide (DMVBPO), and 2,4,6-trimethylbenzoyl(phenyl-4-vinylphenyl)phosphine oxide (TMBVPO). They were copolymerized with *N*-vinylpyrrolidone (NVP) or dimethylacrylamide (DMA) to form poly(VBPO-*co*-NVP) [PPI-1a], poly(VBPO-*co*-DMA) [PPI-1b], poly(DMVBPO-*co*-DMA) [PPI-2] and poly(TMBVPO-*co*-DMA) [PPI-3] respectively.

In the case of the above-described photoinitiating monomers, benzoyl radicals bearing a polymerizable group (VBPO or DMVBPO) could copolymerize with co-existing radical polymerizable resin monomers, thereby preventing the migration of benzoyl radicals from the polymers. An additional advantage of these photoinitiating monomers is that they could be activated by visible light.

Visible light reactivity and stability of polymeric photoinitiators bearing APO moiety in HEMA solution

To investigate the photopolymerization of these synthesized polymeric photoinitiators (*i.e.*, PPI-1a, PPI-1b, PPI-2, and PPI-3) under blue light (visible light) irradiation, photocalorimetric studies were performed using a DSC (photo-DSC) in combination with a blue

Fig. 18 Synthesis of anthraquinone derivative, which comprised a polymerizable moiety (HTAQ-MEI), by a reaction between 2-(2-hydroxyethylthio)-9,10-anthraquinone (HTAQ) and 2-methacryloyloxyethyl isocyanate (MEI)⁵³⁾.

Fig. 19 Structural formulas of vinyl-functional phosphine oxide photoinitiating monomers⁴⁰⁾. Full names of VBPO, DMVBPO, TMBVPO, and their copolymers with NVP or DMA are given in Table 1.

light dental gun (Heliolux DLX, Vivadent, Liechtenstein). HEMA, photoinitiator, and in some cases, water were mixed in subdued visible light.

Figure 19 also presents the characteristics of these synthesized polymeric photoinitiators. Results showed that all the synthesized polymeric photoinitiators were useful in visible light bleaching photoinitiators. On photoinitiator stability, PPI-1a was not stable in HEMA solution, whereas VBPO-dimethylacrylamide copolymer (PPI-1b) was stable in HEMA but not stable in aqueous solution. PPI-2 was both soluble and stable in water up to 22 months.

On polymerization efficiency, PPI-1a was as effective as trimethylbenzoyl diphenylphosphine oxide (TMDPO). PPI-2 exhibited greater polymerization efficiency in HEMA/water mixtures than PPI-3. PPI-2 and PPI-3 acted as self-crosslinking species, resulting

Fig. 20 Structural formula of a polymeric photoinitiator bearing side-chain benzoyl diphenylphosphine oxide moieties and its α -cleavage photoinitiation⁵⁴. Full names of poly(VBPO) and poly(VBPO-co-MMA) are given in Table 1.

Fig. 21 Structural formula of a polymeric photoinitiator with pendant 2,6-dimethylbenzoyl-diphenylphosphine oxide moieties⁵⁵. Full names of poly(ADBA) and poly(ADBA-co-BA) are given in Table 1.

Fig. 22 Structural formula of radical polymeric photoinitiator bearing camphorquinone moieties¹. Full names of MCQ and poly(MCQ-co-BM-co-DMAEM) are given in Table 1.

in formation of hydrogels, and that PPI-3 was more effective than PPI-2 in this aspect. PPI-2 was very effective in forming hydrogels based on poly(ethylene glycol) diacrylate.

Synthesis and kinetics of polymeric photoinitiators bearing side-chain APO pendant

Angiolini *et al.*⁵⁴ synthesized polymeric photoinitiators

bearing side-chain benzoyl diphenylphosphine oxide moieties [poly(VBPO) and poly(VBPO-co-MMA)] prepared by a reaction between poly(4-vinylbenzoic acid) [poly(VBA)] or [poly(VBA-co-MMA)] and thionyl chloride, followed by a reaction with methoxydiphenylphosphine (Fig. 20).

As for polymeric photoinitiators with pendant 2,6-dimethylbenzoyl diphenylphosphine oxide moieties [poly(ADBPO) or poly(ADBPO-co-BA)], they were synthesized by reacting homopolymer of 4-acryloyloxy-2,6-dimethyl benzoic acid [poly(ADBA)] or ADBA/*n*-butyl acrylate (BA) copolymers [poly(ADBPO-co-BA)] with thionyl chloride, followed by a reaction with methoxydiphenylphosphine⁵⁵ (Fig. 21).

On photoinitiation activity, poly(VBPO-co-MMA)s exhibited markedly improved activity than analogous aliphatic polymeric systems bearing the acylphosphine oxide moiety in the side chain⁵⁴. On stability to daylight, poly(ADBPO-co-BA) exhibited appreciably higher stability than TMDPO, which is reported to be the most stable commercial member of this class of photoinitiators⁵⁵.

Synthesis and kinetics of polymeric photoinitiators bearing side-chain camphorquinone moiety

In a study by Angiolini *et al.*¹, novel polymethacrylic photoinitiators bearing the photosensitive camphorquinone moiety in the side chain, D,L-10-methacryloyloxy-camphorquinone (MCQ) (Fig. 22), was synthesized by the reaction between D,L-10-hydroxycamphorquinone and methacryloyl chloride. Monomer MCQ was copolymerized with 2-dimethylaminoethyl methacrylate (DMAEM) in different ratios to give the corresponding polymeric derivatives, poly(MCQ) and poly(MCQ-co-DMAEM). To improve solubility, copolymer derivatives poly(MCQ-co-BM) and poly(MCQ-co-BM-co-DMAEM) were further synthesized using the butyl methacrylate (BM) comonomer.

An equimolar 1,6-hexanediol diacrylate (HDDA)/butyl acrylate (BA) mixture (50/50, mol%) containing 1 mol% of camphorquinone moiety with an equimolar amount of amine was polymerized under a nitrogen-rich atmosphere by irradiation from a high-pressure mercury lamp (>400 nm). Table 11 presents the UV-VIS properties and kinetic data of the synthesized polymeric photoinitiators bearing the camphorquinone moiety, as a function of the photoinduced crosslinking polymerization.

In terms of UV-VIS spectral data, the maximum absorption wavelengths (λ_{max}) of CQ, synthesized poly(MCQ-co-DMAEM) and poly(MCQ-co-BM-co-DMAEM) were 483, 469, and 469 nm respectively. The molar extinction coefficients (ϵ_{max} , 1 mol⁻¹ cm⁻¹) of these photoinitiators were 39.0, 35.8, and 35.6 respectively. Among the investigated photoinitiators, poly(MCQ-co-BM)/DMAEM exhibited the best photoinitiation activity although it had a slightly higher induction time (Table 11).

Nonetheless, for copolymeric photoinitiators

Table 11 UV-VIS properties and kinetic data of photoinitiation activity by polymeric and low-molecular-weight photoinitiator systems based on camphorquinone in the photopolymerization of an equimolar HDDA/BA mixture upon irradiation above 400 nm¹⁾

Photoinitiators	UV-VIS properties		T_{ind} (sec)	$t_{1/2}$ (sec)	Conversion (%)
	λ_{max}	ϵ_{max}			
CQ	483	39.0	63	515	60.1
Poly(MCQ-co-BM)/DMAEM	469	35.8	15	64	85.2
Poly(MCQ-co-BM)/poly(DMAEM)	469	35.8	42	152	85.4
Poly(MCQ-co-BM-co-DMAEM)	469	35.6	25	132	87.0

Photoinitiator concentration in the acrylic formulation: 1.0 mol% of camphorquinone moiety with an equimolar amount of amine when used in combination. The values of λ_{max} and ϵ_{max} were not indicative of DMAEM and poly(DMAEP). T_{ind} : Induction time of the curing process at 1% conversion of double bond. $t_{1/2}$: Time required for reaching 50% conversion of the HDDA/BA mixture. Conversion: Double-bond conversion after 600 seconds of irradiation time. Full names of HDDA, BA, CQ, DMAEP, Poly(DMAEM), Poly(MCQ-co-BM), Poly(MCQ-co-BM-co-DMAEM), λ_{max} and ϵ_{max} are given in Table 1.

containing the photoreactive moieties of camphorquinone and tertiary amine in the side chain, the general trend is a decrease in efficiency in terms of induction time and polymerization rate, probably because of steric hindrance to exciplex formation¹⁾. The close proximity of the photosensitive moieties to the macromolecular backbone most probably reduced their mobility, thus favoring recombination reactions between the active radical species. Moreover, since an inordinate number of steps are needed for their syntheses, it seemed that these copolymeric photoinitiators would remain limited to industrial application.

In conclusion, for the copolymeric photoinitiator containing both photoreactive camphorquinone and synergistic tertiary amine moieties in the side chain, the efficiency in terms of induction time and polymerization rate decreased, probably because of steric hindrance to exciplex formation¹⁾. The close vicinity of the photosensitive moieties to the macromolecular backbone most probably reduced their mobility, thus favoring recombination reactions between the active radical species. Moreover, since an inordinate number of steps are needed for their syntheses, it seemed that these copolymeric photoinitiators would remain limited to industrial application.

Upon completion of this review paper, a myriad of photoinitiators would have been developed. However, the scope and limitation of this paper was to review recent studies on radical photopolymerization initiators, which were used in the design of light-curing dental adhesives and resin composites, by collating information of related studies on these photoinitiators.

CONCLUSION

Within the limitations of this review paper, the key conclusions drawn are as follows:

1. No significant differences in degree of conversion (DC) ($p > 0.05$) were observed between BAPO and CQ/amine system.

2. Newly synthesized 7,7-dimethyl-2,3-dioxobicyclo [2.2.1]heptane-1-carbonyldiphenyl phosphine oxide (DOHC-DPPO=CQ-APO) possessed two maximum absorption wavelengths (λ_{max}) at 350–500 nm [372 nm (from APO group) and 475 nm (from CQ moiety)].
3. CQ-APO-containing resins exhibited good photopolymerization reactivity, excellent color tone, relaxed operation time, and high mechanical strength.
4. A water-soluble photoinitiator APO-Na with crown ether improved the adhesion of single-step hydrophobic bonding resin to ground dentin, and an experimental HEMA-free self-etching adhesive exhibited strong adhesion to both ground enamel and dentin.
5. For copolymeric photoinitiators containing the photoreactive moieties of camphorquinone and tertiary amine in the side chain, there was a discernible decrease in efficiency in terms of induction time and polymerization rate, probably because of steric hindrance to exciplex formation.

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