UNIVERSITY OF BIRMINGHAM

Increased rates of photopolymerisation by ternary type II photoinitiator systems in dental resins

Lima, Adriano Fonseca; Salvador, Marcos Vinicius Oliveira; Dressano, Diogo; Saraceni, Cintia Helena Coury; Gonçalves, Luciano Souza; Hadis, Mohammed; Palin, William M

Document Version
Peer reviewed version

Link to publication on Research at Birmingham portal

Publisher Rights Statement:
Checked for eligibility: 26/06/2019

Increased rates of photopolymerisation by ternary type II photoinitiator systems in dental resins

*Adriano Fonseca Lima [a], Marcos Vinicius Oliveira Salvador [a], Diogo Dressano [b], Cintia Helena Coury Saraceni [a], Luciano Souza Gonçalves [c], Mohammed Hadis [d], William M. Palin [d]

[a] Dental Research Division, Paulista University, Sao Paulo, Brazil. Rua Doutor Bacelar, 1212. CEP: 04026-002. Sao Paulo – Brazil. lima.adf@gmail.com (A. F. Lima); marcosviniciussalvador@gmail.com (M. V. Salvador); cintiahcsaraceni@gmail.com (C. H. Saraceni)

[b] Department of Restorative Dentistry, Piracicaba Dental School, State University of Campinas, Piracicaba, Brazil. Av Limeira, 901 Mail Box 52, Piracicaba, Sao Paulo 13414-903 Brazil. diogodressano@gmail.com

[c] Department of Conservative Dentistry, Federal University of Rio Grande do Sul School of Dentistry, Av. Paulo Gama, 110 - Farroupilha, Porto Alegre - RS, 90040-060. Porto Alegre, RS, Brazil. goncalves1976@yahoo.com.br

[d] Biomaterials Unit, University of Birmingham, College of Medical and Dental Sciences, School of Dentistry, St Chad's Queensway, Birmingham B4 6NN, UK. M.Hadis@bham.ac.uk (M. Hadis); w.m.palin@bham.ac.uk (W. M. Palin)

*Author to whom correspondence should be addressed. Present address:

Prof. Dr. Adriano Fonseca Lima

Dental Research Division

School of Dentistry – Paulista University

Rua Doutor Bacelar, 1212. CEP: 04026-002

Sao Paulo - Brazil

Tel: +55-11 5586-4000. E-mail: lima.adf@gmail.com

Increased rates of photopolymerisation by ternary type II photoinitiator systems in dental resins

Abstract

To evaluate the effects of Type I and Type II photoinitiator systems on curing efficiency, degree of conversion (DC) and chemico-physical properties of resin based materials. A comonomer base containing 50%wt 2.2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (bis-GMA) and 50%wt triethyleneglycol dimethacrylate (TEGDMA) was formulated with either 0.5 or 1mol% of Type II camphoroquinone (CQ), Type I monoacylphosphine oxide (MAPO) or bis-acylphosphine oxide (BAPO) photoinitiators. The Type II system was either a binary (1: 2 CQ:amine) or ternary system (1: 2 CQ:amine + 0.5 mol% DPI). Degree and rate of polymerization was measured by Fourier Transform Infrared Spectroscopy (FTIR). Knoop micro-hardness prior to and following ethanol immersion was assessed. Flexural strength and modulus was measured under three-point bend test. Water sorption and solubility was also evaluated. The photoinitiator absorption spectra and the total absorbed energy per unit volume (E_{abs}) for 0.5mol% photoinitiator in each material was calculated. Despite the reduced total absorbed energy per unit volume for CQ based systems, ternary Type II system significantly improved curing efficiency (P<0.05) compared to both Type I photoinitiators and degree of conversion compared to MAPO only, whilst exhibiting comparable mechanical and physical properties compared to both Type I based materials at equivalent molar concentrations of photoinitiator (P>0.05). Ternary Type II systems is an efficient alternative to improve the polymerization of resin materials, promoting similar or even better properties than Type I initiators. DPI can increase the reactivity of CQ systems and promote polymerization rates superior than Type I photoinitiators.

1. Introduction

Photo-activated resin composite restoratives, resin-based luting composites and adhesives are widely used during the placement of dental restorations due to the many advantages including improved working time, improved tissue colour matching and the ability to command cure *in situ* compared with chemically cured materials. Polymerisation of resin-based dental materials commonly involves a combination of the Type II dye-based photoinitiator, camphoroquinone (CQ), which has an absorption band between ~400-490 nm (λ_{max}: 469 nm) and an amine tertiary co-initiator allowing polymer crosslinking by photons of visible (blue) light. The photoinitiator concentration and its ratio with the coinitiator are optimized to obtain high degree of conversion (Guimaraes et al., 2014).

Previous research of Type I photoinitiators, such as monoacylphosphine oxide (MAPO - λ_{max}: 380 nm), and phenylbis (2,4,6-trimethylbenzoyl)-phosphine oxide (BAPO - λ_{max}:: 370 nm) have aimed to improve material properties in experimental and commercial dental resin composites (Meereis et al., 2014; Palin et al., 2014; Randolph et al., 2014b). Type I photoinitiators allow photopolymerisation by shorter wavelength, higher energy photons of visible (violet) light. These initiators provide 1) significantly higher molar absorptivities compared with CQ (MAPO ~520 $mol^{-1} L^{-1} cm^{-1}$; BAPO ~300 $mol^{-1} L^{-1} cm^{-1}$; and CQ ~28 $mol^{-1} L^{-1} cm^{-1}$) (Neumann et al., 2005) , which may increase curing efficiency, 2) low pigmentation due to shorter UV wavelength range absorption, which may improve tissue color matching (de Oliveira et al., 2015) and, 3) elution of residual monomers is reduced as crosslink density of the parent resin is increased (Randolph et al., 2014a). The photochemical reaction mechanism of Type I photoinitiators generates more active radicals, higher photo-reactivity and increased quantum yield, (MAPO/BAPO: ~0.55.0.59 [17]; CQ: ~0.10) compared with the bimolecular CQ/amine chemistry (Chen et al., 2007; Neumann et al., 2005; Neumann et al., 2006)..

The advent of materials that utilise short wavelength Type I photoinitiators has also seen the introduction of LED light curing units (LCUs) with multiple diodes that provide a broader range of output wavelengths needed to coincide with the absorption of Type I and Type II photoiniator systems. However, the spectral optical power distribution of violet and blue light in commercial LCUs typically favours longer wavelength blue diodes since CQ is by far the most common photoinitator used in commercial resin composites. This fact can be true also due to the potential cytotoxic effects

of short UV-visible wavelengths and high energy photons on ocular, oral and other human tissue (Glickman, 2011) (notwithstanding the significant blue light hazard of high power modern LCUs (Nakamura et al., 2018)). Furthermore, whilst these LCUs exhibit differences in spectral power distribution, non uniform spatial power due to diode alignment may lead to inhomogeneous curing properties (Harlow et al., 2016; Price et al., 2010).

Whilst the photopolymerisation process of Type I initiators involves the absorption of short wavelength, high energy violet light, and subsequent excitation to singlet state and photochemical cleavage of carbon-phosphorus bonds, the photopolymerisation of Type II photoinitiator based materials involves the absorption of visible blue light by the carbonyl group of CQ and transition into a triplet state via excitation into a singlet state. The subsequent steps that involve hydrogen abstraction from the co-initiator and radical formation are highly dependent upon the co-intiator type, the concentration and its structure. Generally, aromatic tertiary amines such as ethyl-4-dimethylaminobenzoate (EDMAB) are considered more efficient than linear chain tertiary amines such as dimethylaminoethyl methacrylate (DMAEMA) due to a greater localisation of electrons through aromatic groups allowing a more efficient electron transfer process and reduces the possibility of back electron transfer. Back electron transfer reverses the excited state of the photoinitiator and restores the donor and acceptor to their original oxidation levels which retards the hydrogen abstraction process and the generation of photoinitiator radicals which ultimately reduces the efficiency of photopolymerization (Andrade et al., 2016; de Oliveira et al., 2015).

Diphenyliodonium salts (DPI) has been used for years to improve the polymerization process of radicalar and cationic reactions (Cook and Chen, 2011; Oxman et al., 2005; Timpe and Rajendran, 1991). In addition, DPI photosensitisers have been shown to improve efficency of CQ/amine photoinitiator systems by reducing the back electron transfer process, leading to remarkable improvements in degree of conversion, rate of polymerization and depth of cure (Andrade et al., 2016; Goncalves et al., 2013; Ogliari et al., 2007). The use of DPI photosensiters to improve curing efficiency of resin based materials rather than alternative photoinitiators has several advantages. Firstly, conventional LED LCUs that have single wavelengths and more symmetrical beam profiles may provide a more uniform cure. Secondly, it may be possible to reduce the photoinitiator and amine co-initiator concentrations thus improving aesthetics and cytotoxicity of conventional materials. Lastly,

improved efficiency may reduce the curing time which may translate into reduced restoration placement time which is higly desired clinically.

Previous studies analysing the efficiency of Type I initiators as MAPO and BAPO indicanting the best performance of these agents compared to CQ containing resins did not use DPI as co-initiator (Bertolo et al., 2017; Schneider et al., 2012a), restricting the efficiency of the polymerization system and limiting the understanding of CQ systems in comparison to Type I initiators. In addition, some studies demonstranting the best performance of type I initiators compared to CQ usually used DMAEMA as co-initiator (Leprince et al., 2011; Palin et al., 2014; Randolph et al., 2014a; Randolph et al., 2014b), which can also reduce the efficiency of the system compared to the aromatic amine EDMAB, as described in previous studies (Andrade et al., 2016; Bacchi et al., 2018; de Oliveira et al., 2015). Therefore, the aim of the present study is to evaluate the influence of different initiator systems (CQ/EDMAB; CQ/EDMAB/DPI, MAPO and BAPO) on polymerization process (degree and rate of polymerization) and chemico-physical properties (flexural strength and modulus, water sorption and solubility; Knoop microhardness) of experimental filled resins. The hypothesis is that the use of a ternary Type II system will significantly improve the rate of polymerization and degree of conversion whilst exhibiting comparable mechanical and physical properties to Type I based materials at equivalent molar concentrations of photoinitiator.

2. Materials and Methods

2.1. Material preparation

Unfilled resins were prepared at a 1:1 mass ratio of 2.2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane (Bis-GMA) and triethyleneglycol dimethacrylate (TEGDMA) (Esstech Inc., Essington, PA, USA). Butylated hydroxytoluene (BHT) (Esstech Inc.) (0.1 mol%) were added as inhibitor and the mixture was blended and homogenized for 1 h at room temperature (25° C) with a magnetic stirrer (2000 rpm). The monomer base was aliquoted into 8 fractions and groups were formed according to the type and concentration of initiator system (Table 1). Ethyl dimethilamino benzoate (EDMAB) 2mol% was used as co-initiator for the resins containing CQ (1mol%). Each formulation was loaded with 60wt% of 0.7-µm average size silanated barium borosilicate glass fillers (Esstech Inc). The experimental composites were mixed and homogenized using a dual asymmetric centrifuge at 3500 rpm (Speed mixer, Flack- Tek, USA). All chemicals were

used without further purification. <mark>The composites homogeneity was checked after mixing and before specimens' preparation for each analysis</mark>

Table 1 – Experimental groups established according to the initiator system used.

Group	Initiator System
G1	CQ 0.5mol%
G2	CQ 1mol%
G3	CQ 0.5mol% + o.5mol% DPi
G4	CQ 1mol% + o.5mol% DPi
G5	BAPO 0.5mol%
G6	BAPO 1mol%
G7	MAPO 0.5 mol%
G8	MAPO 1mol%

2.2. Spectral irradiance and absorption

A dual peak light curing unit (LCU, Bluephase G2, Ivoclar Vivadent AG, Schaan, Liechtenstein) was used for all light curing procedures. The LCU was spectroradiometrically characterised using calibrated fiber coupled spectrophotometer device (MARC[®]; Bluelight Analytics Inc., Halifax, NS) to obtain information on absolute irradiance and wavelength. The tip of the LCU (10mm) was positioned centrally above the 4mm upper sensor of the MARC RC at 0mm distance. The spectral irradiance was subsequently recorded using MARC RC software (Halifax, Canada)

2.3. Photoinitiator absorption

Absorption spectra of MAPO, BAPO, and CQ were measured in methyl methacrylate (Sigma-Aldrich) using a fibre coupled USB4000 spectrometer. The spectrometer was calibrated using a broadband light source (Range 215-2500nm; DH2000, Ocean Optics UK) in absorbance mode with methyl methacrylate as the reference. Standard cuvvetts were filled with photoinitiator solutions and the

spectral absorbance was recorded. Spectral absorbance was converted into molar absorptivity using Beer-Lamberts law.

2.4. Total absorbed energy per unit volume

The total absorbed energy per unit volume (E_{abs}) for 0.5mol% photoinitiator in each material (according to the CIE/ISO definition) was calculated using the spectral absorbance of the photoinitiators and the spectral irradiance of the Bluephase G2 light according to the following equation:

$$E_{abs} = \int_{520}^{380} Irr(\lambda)\mu_a(\lambda)d(\lambda). \qquad \text{Equation 1}$$

where $Irr(\lambda)$ is the spectral irradiance of the Bluephase G2 light and μ_a is defined by equation 2:

$$\mu_a(\lambda) = \frac{A(\lambda)(Ln\ 10)}{d} \qquad \text{Equation 2}$$

where $A(\lambda)$ is the spectral absorbance of the photoinitiators and d is the optical path length.

2.5. Real-time polymerization

Degree of conversion (DC) was assessed in real time by measureing aliphatic (1638cm^{-1}) and aromatic (1608cm^{-1}) carbon double bond absorption at the lower surface of specimens (5mm diameter, 1mm thick) using a Fourier Transform infra-red attenuated total reflectance (FTIR-ATR, Nicolet 6700, Thermo Scientific, Pittsburgh, PA, USA) method. The spectrometer was fitted with a liquid nitrogen cooled MCT detector to improve the signal to noise ratio whilst maintaining high acquisition rates (0.2s^{-1}), . A silicon mold (5 mm inner diameter x 1 mm thick) was fixed onto the ATR plate to ensure concentric allignment and reproducible specimen dimensions. Specimens (n=3) were placed centrally over the diamond crystal which created an indent into the lower surfaces of the specimens of 2.65mm in diameter and 0.33mm deep, and the upper surfaces were covered with mylar strips. The specimens were subsequently light cured for 40s using a a Bluephase G2 light source, to obtain the maximum polymerization of each formulation, and FTIR spectra (3 scans averaged per spectrum, 16 cm^{-1} resolution) for a total of 90s. The conversion measurements were

based on the peak height ratios between the carbon double bond (aliphatic) stretching mode

(1637cm^{-1}) and isosbestic point (aromatic: typically 1608cm^{-1}) according to the equation 3:

$$Conversion\ \% = \frac{aliphatic/isosbestic\ (peak\ areas\ of\ polymer)}{aliphatic/isosbestic\ (peak\ areas\ of\ monomer)} \qquad \text{Equation 3}$$

The rate of polymerisation was calculated as a differential function of degree of conversion and

time and smoothed using a 5 point rolling average.

2.6. Knoop Hardness

Disc-shaped specimens (5 mm diameter, 1 mm thick) were prepared in silicon molds. The

experimental material was inserted in the mold and a Mylar strip was positioned above the resins

before light activation, using a clinical viable time of 20s, which promoted optimal cure of all

formulations tested according the real time polymerization analyzes performed previously. Following

irradiation, the Mylar strip was removed and the samples were stored in dark for 24h at room

temperature before tested. Indentations (n=5) were made centrally, with 100 µm distant between

each other, on the upper surface out of each specimen using a Knoop Hardness tester (HMV 2,

Shimadzu, Tokyo, Japan) using a 50 g load and 15 s dwell time. Subsequently, specimens were

incubated for 24 h in 100% ethanol at 37° C; and the hardness re-measured by creating new indents

(n=5) centrally on the upper surface (100 µm distant from the first indents).

2.7. Water Sorption (WS) and Solubility (S)

For water sorption and solubility, silicone moulds were used to prepare the discs (5 mm

diameter, 1 mm thick). The experimental resins were placed into the silicon moulds and a Mylar strip

was used to cover the upper surface. After polymerization (20s), the specimens (n=5) were stored in

plastic tubes at 37°C in a desiccator.

2.7.1. Water Sorption

The samples were weighed daily during the drying period using an analytical balance

(Discovery DV215CD, Ohaus Corporation, Pine Brook, NJ, USA) until obtain a constant weight

The diameter and thickness were measured to calculate the sample volume (mm^3). After obtain m1, the samples were individually stored in plastic tubes containing distilled water (1.5 ml) and stored at 37 ° C for 21 days. The samples were then removed from the incubator and lightly dried with absorbent paper and weighed to verify the mass after immersion in water (m2).

Water Sorption (WS) = ((m2-m3))/V   Equation 4

where m1 is the initial weight before immersion in distilled water, m2 is the mass after immersion in distilled water and V is the volume of the m1 sample in mm^3.

2.7.2. Solubility

The samples were then placed in desiccator at 37 ° C and were daily weighed until obtain a constant weight (m3). The water sorption and solubility were calculated in g/mm^3, by the following equation:

Solubility= ((m1-m3))/V   Equation 5

where m3 is the mass after the second drying cycle in mg;

2.8. Flexural strength (FS) and modulus (E)

Bar-shaped specimens (25 mm length, 2 mm width and 2 mm height) were prepared for three-point bending measurements (n = 12) using a stainless steel-mould. A Mylar strip was fixed below the stainless steel matrix and then the mould was filled with the experimental resin before placing a second mylar strip above the resin. The bar shaped specimes were polymerized used a Bluephase G2 light source with the tip positioned centrally and flat against the axis of the bar with five successive overlapping steps (5 x 20s irradiations) originating from the centre of the specimen.

The dimensions of the beams were measured using a digital caliper (Mitutoyo, Tokyo, Japan) immediately. The three point bending experiments were performed in a universal testing machine (2000RK, Kratos, São Paulo, Brazil), at a crosshead speed of 1mm/min with 50 kgf load cell (distance between the supports was 20 mm). The flexural strength (FS) was calculated according to the equation below:

$$FS = \frac{3FI}{2bh^2} \qquad \text{Equation 6}$$

where F is the the maximum load (Newtons) required to break the specimen, l is the distance between the supports (20 mm), b is the average width of specimen and h is the average thickness.

The flexural modulus (E) for each sample was calculated from the linear portion of the stress-strain curve, corresponding to the elastic deformation of the material, using the formula:

$$E = \frac{\Delta F}{\Delta Y} \; x \; \frac{I^3}{4bh^3} \quad \text{Equation 7}$$

ΔF / ΔY/ = force change (ΔF) per unit change in deflection at the center of the sample (ΔY);

L = distance between the supports (20 mm);

b = average width of the sample;

h = was the average thickness.

2.9. Statistical analysis

Prior to statistical analysis, the data was analyzed for normality and homogeneity of variance. One-way Analysis of Variance (ANOVA) and Tukey post-hoc comparisons (P<0.05) was performed on the datesets for DC, rate of polymerization, KHN, flexural and elastic modulus, as well as water sorption. The solubility results were analysed by Kruskal-Wallis test. All statistical analysis was performed using the software SAS (SAS Institute, North Caroline, USA) using a 95% confidence level.

3. Results

The molar absorptivity of the photoinitiators and absolute irradiance of the curing unit are presented in Figure 1. The significant difference in molar absorptivity of camphorquinone and the type I initiators at the peak absorption wavelengths (CQ: λ_{470} = 29.8; MAPO: λ_{380} = 515; BAPO: λ_{370} = 306) is apparent albeit with partial spectral overlap of type 1 initiators with the emission spectra of the Bluephase G2 light.
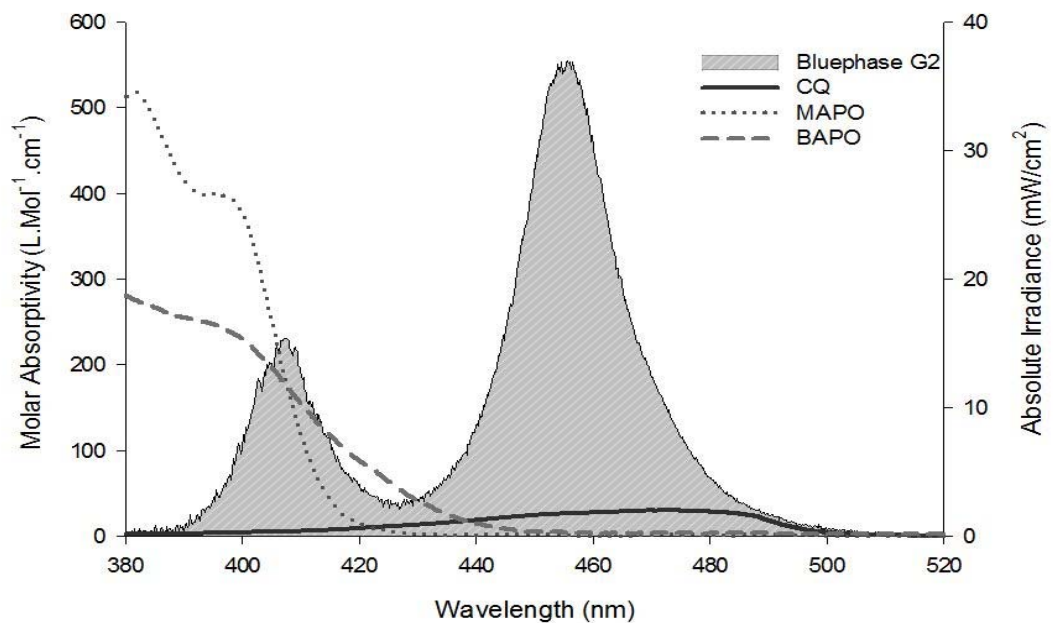
Fig. 1 - Photoinitiator molar absorptivity and absolute irradiance of curing unit used

However, whilst there exists only partial spectral emission/absorption overlap with the LCU and and Type I photoinitators, at the same molar concentration of initiators, Type I photoinitiators exhihibit a significantly higher effective value of total absorbed energy per unit volume compared to the Type II photoinitiator CQ, (1.06, 2.46 and 2.34 J/cm^3 for CQ, MAPO and BAPO respectively) although the absorbed energy by CQ spans a broader spectral range with a small but significant contribution from violet wavelengths (Figure 2) . Doubling the concentration of CQ also doubles the effective value of total absorbed energy per unit volume (2.12J/cm^3). The spectral absorbed energy per unit volume at equivalent concentrations is shown in Figure 2.
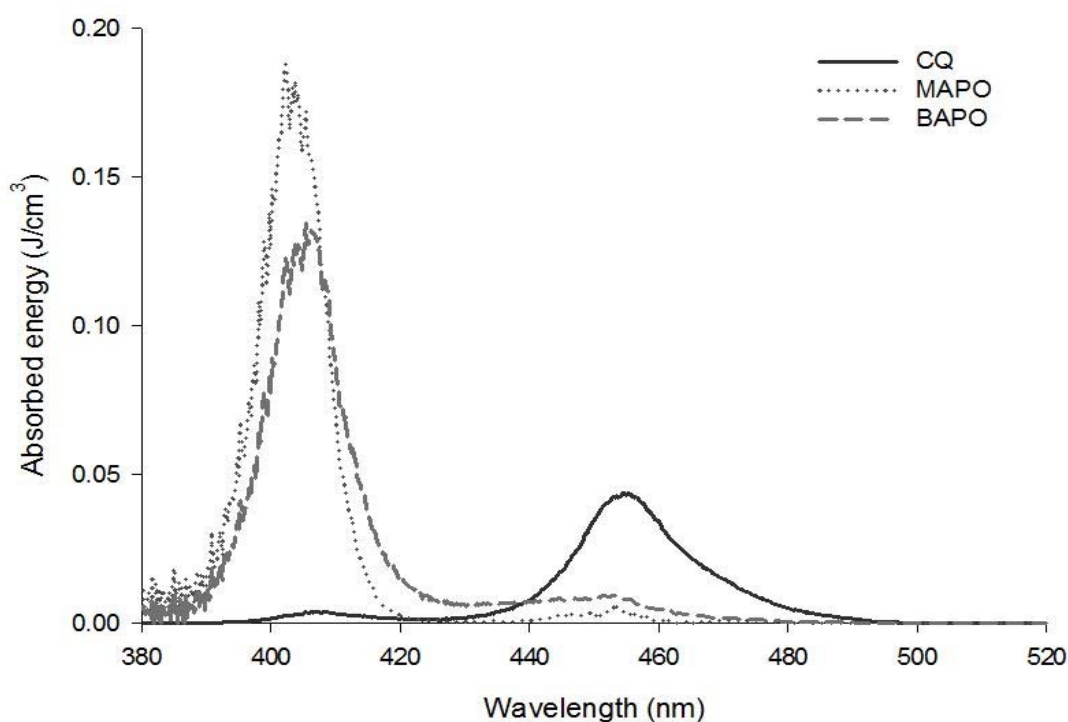
Fig. 2: The spectral absorbed energy per unit volume at equivalent molar concentrations (0.5mol%) for Type I photoinitiators, MAPO and BAPO, and the Type II photoinitiator, CQ. It can be seen that whilst the optical power of the Bluephase G2 light favours longer blue wavelenths (Figure 1), those wavelengths are weakly absorbed by the Type II photoinitiator, CQ, compared to the shorter violet wavelengths by Type 1 photoinitiators.

Significant differences in DC were measured for each photoinitiator system at equivalent concentrations ($p < 0.0001$; Table 2). Resins which contained the Type I photoinitiator BAPO exhibited the highest DC (80-85%) followed by resins containing a ternary Type II photoinitiator system (78-79%), the Type 1 MAPO system (74-76%) and finally the binary Type II CQ photoinitiator system (72-77%; Table 2). For the same photoinitiator system, doubling the concentration from 0.5 mol% to 1.0

mol% increased conversion except in the ternary Type II photoinitiator system. However, whilst

resins containing the Type I BAPO system exhibited the highest DC, the ternary Type II CQ based

system exhibited the highest rates of polymerisation whilst the binary CQ based resins exhibited

significantly lowest polymerisation rates (P<0.001). The real time degree of conversion and rate of

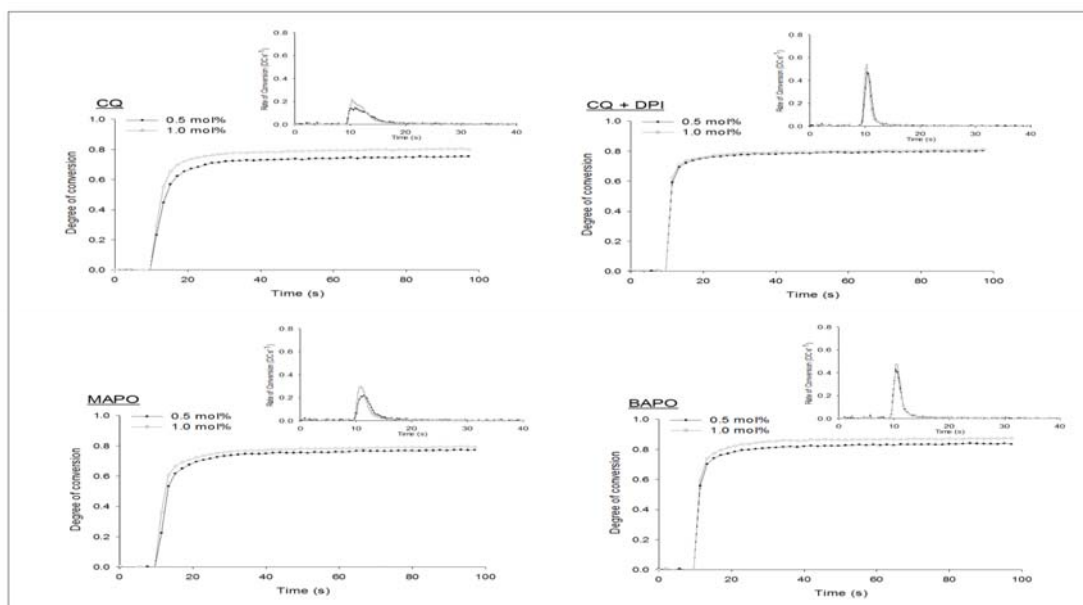polymerization can be observed at Figure 3.

Fig. 3 – Real time degree of conversion (a) and rate of the polymerization (b) of groups tested.

Table 2 – Means and (standard-deviations) of degree of conversion (20s) and maximum rate
of polymerization of experimental groups

	DC (%)	Max. RP (%/s)
CQ 0.5 mol%	71.81 (0.48) D	18.07 (0.18) F
CQ 1 mol%	77.31 (3.06) B	26.00 (2.27) E
CQ 0.5 mol% + DFI	77.93 (0.55) B	51.44 (1.14) BC
CQ 1 mol% + DFI	78.7 (1.48) B	62.72 (2.18) A
BAPO 0.5 mol%	80.8 (1.63) AB	47.78 (2.86) C
BAPO 1 mol%	85.42 (2.96) A	52.98 (1.78) B
MAPO 0.5 mol%	73.72 (0.48) C	23.66 (0.47) E
MAPO 1 mol%	76.41 (0.57) B	31.85 (1.05) D

One-way ANOVA and Tukey's Test. Different letters indicate statistical difference. α=0.05.

The upper surface hardness of samples were also significantly influenced by photoinitiator type where binary Type II CQ based materials exhibited the significantly lowest hardeness values (P<0.05). However, the significantly highest hardness values were measured for ternary Type II CQ based systems and were significantly higher than Type I MAPO and BAPO based system (P<0.05; Figure 4). The concentration of photoinitiator also had a significant influence on surface hardness for Type I photoinitiators and the binary Type II CQ based system. However, for the ternary Type II CQ based system, the increase in CQ concentration did not significantly influence KHN (p>0.05). Ethanol immersion significantly reduced KHN in all experimental groups by ~50% with no significant differences in percentage reduction among the groups (p>0.05). Thus, although at lower KHN, the trends following ethanol immersion were similar to the trends prior to ethanol immersion.
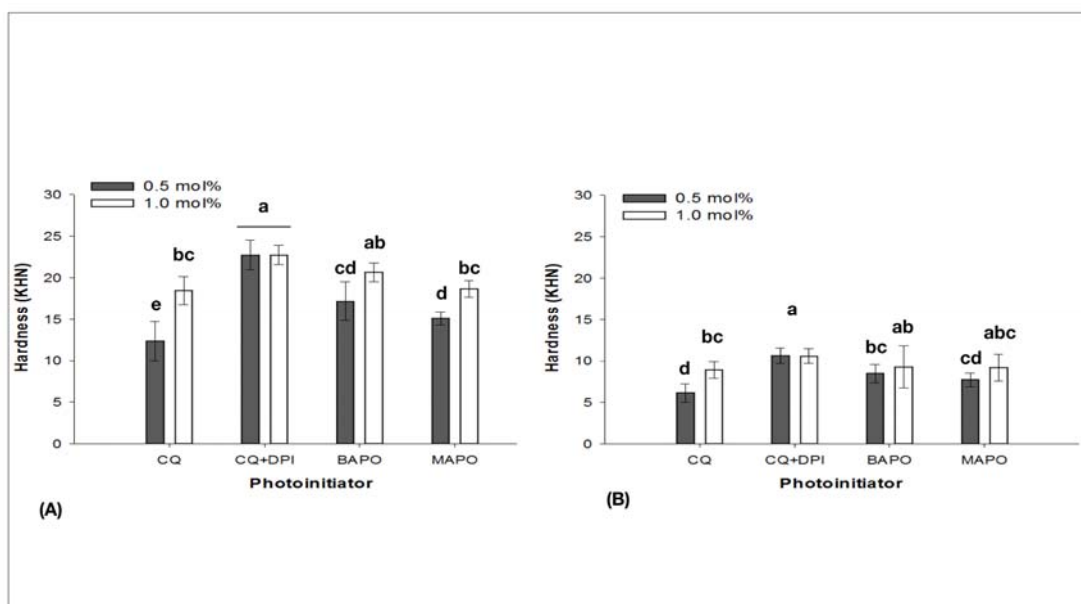

Fig. 4 – Results obtained after microhardness evaluation (baseline) [a] and after ethanol immersion [b]. One-way ANOVA and Tukey's Test. Different letters indicate statistical difference. α=0.05.

Statistical analysis on the the influence of photoinitiator system and concentration (Figs. 5 b, c and d, respectively) did not reveal any significant difference for water sorption (p=0.1275), solubility (p=0.3266) and flexural strength (p=0.4801). In terms of flexural modulus (*E*), significantly lowest values were measured for resins containing the Type II binary system at a concentration of 0.5mol%

(P<0.05; Fig. 5 a). Excepting resins containing CQ 0.5mol% without DPI, all resins had statistically similar flexural modulus.
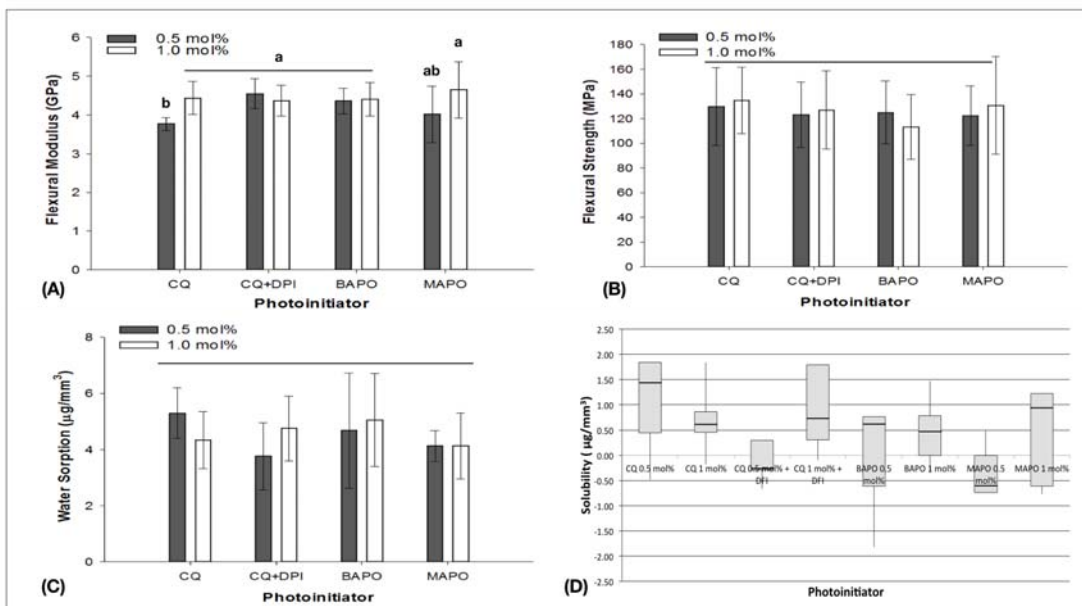

Fig. 5 – Graphical representation of flexural modulus (a) and strength (b), water sorption (c) and solubility (d) of experimental groups. One-way ANOVA and Tukey's Test (flexural modulus and strength, water sorption). Medians e (interquartil-intervals 25%;75%) for solubility evaluation (Kruskal-Wallis, SNK). Different letters indicate statistical difference. α=0.05.

4. Discussion

Since the use of a ternary Type II system (CQ, Amine and DPI) significantly improved curing efficiency compared to both Type I photoinitiators and degree of conversion compared to MAPO only, whilst exhibiting comparable mechanical and physical properties compared to both Type I based materials at equivalent molar concentrations of photoinitiator, the hypothesis was partially accepted.

The ability of photoinitiators to absorb light which is generally defined by the molar absorptivity is a major factor that will influence the polymerisation reaction in terms of kinetics and final polymer conversion (Leprince et al., 2011; Neumann et al., 2005). Here, the molar absorptivity of the photoinitiators significantly differed at the peak absorption wavelength and was generally higher for the Type 1 initiators (λ_{380}=515 L.mol^{-1} cm^{-1} and λ_{370}=306 L.mol^{-1} cm^{-1} for MAPO and BAPO respectively; Figure 1) compared to the Type 2 initaitor, CQ (λ_{469}=29.8 L.mol^{-1} cm^{-1}; Figure 1). However, whilst molar absorptivity is an important factor for absorption of light, sufficient spectral absorbance/emission overlap between the photoinitiator and LCU must exist for light to be absorbed. The Bluephase G2 light reveals a bimodal distribution of wavelengths centred around 405nm and 460nm (with approximately a 1:3 ratio of optical power output respectively; Figure 1) which only partially overlaps the emission spectra of the Type I photoinitiators (with absorption restricted to wavelengths <440nm). Whilst it could be assumed that the combination of partial overlap and weaker optical power at shorter wavelength range could reduce the total absorbed energy per unit volume, at the same concentration of photoinitiator, the Type 1 initiators in fact exhibit greater total absorbed energy per unit volume compared to CQ (1.06, 2.46 and 2.34 J/cm^3 for CQ, MAPO and BAPO respectively). This is primarily due to the fact that shorter wavelengths of the Bluephase G2 are more efficiently absorbed by the Type 1 initiators compared to the absorption of longer wavelengths by the Type II photoinitiator and is a consequence of the significantly higher molar absorptivity in Type I systems (Figure 1). Thus the quantum yield of photoinitiator conversion, i.e. the ratio of absorbed photons that deplete the photoinitiator, is reportedly greater for MAPO and BAPO (0.55-0.59) (Ganster et al., 2008) compared to 0.10 for CQ-based systems (Chen et al., 2007). Indeed, shorter wavelengths are considered more energetic according to Einstein's equation, which states the energy of a photon is inversely proportional to the wavelength. However, the increased quantum yields for Type I initiators are also likely to be related to the photochemical mechanism by which radicals are formed. For type 1 photoinitiators, photochemical cleavage of the carbon phosphorus bond creates two active radicals for MAPO and four active radicals for BAPO (Ganster et al., 2008; Meereis et al., 2014; Randolph et al., 2014b). However, for the binary type two CQ system, an intermediary step is required prior to radical formation, which only results in one active radical (Guimaraes et al., 2014; Schneider et al., 2012b). Firstly this reduces the rate of radical formation and secondly this results in a

lower yield of total active radicals per mole of photoinitiator molecules. Furthermore so, the excitation of CQ molecules to high energy triplet state represents an unstable state which can undergo back electron transfer to re-generate CQ molecules and is governed by the type and availability of co-initiator and photosensitizer molecules which also has implication for its efficiency (Cook and Chen, 2011; Guimaraes et al., 2014). For example linear chain tertiary amines such as DMAEMA have hydrophilic characteristics, different from those of CQ (Guo et al., 2008), which can hinder the interaction of the two components, reducing the efficiency of the system. In contrast, EDMAB, used in the present study, has an aromatic ring, increased number of C=C bonds, and higher nucleophilicity than DMAEMA which is the ability of a chemical compound to transfer electrons to electrophiles such as excited CQ (de Oliveira et al., 2015; Emami and Soderholm, 2005). These characteristics described previously explain the high degree of conversion obtained by the binary system evaluated. The higher reactivity of used amine compared to DMAEMA improved the efficiency of the system, increasing the degree of conversion to values similar than the Type I initiator MAPO. The better reactivity also explains the difference among the present and previous studies comparing resins containing MAPO and CQ-amine as initiator systems, since the previous studies demonstrating the high superiority of MAPO used the linear chain amine DMAEMA (Palin et al., 2014; Randolph et al., 2014b; Randolph et al., 2016), which promotes lower rate of polymerization and degree of conversion compared to EDMAB containing resins (Andrade et al., 2016).

Despite the existence of several studies evaluating DPI, the effect of this agent on polymerization and properties of resins containing CQ/amine systems compared to Type I initiators was not evaluated. The results shown that, albeit the binary system using EDMAB promote quite similar degree of conversion, DPI resins had a remarkable increase on rate of polymerization, which can be important on clinical situations that resin dental materials are activated with reduced irradiance, such as cementation of indirect restorations and/or restoration of deep cavities.

The photochemistry of photocurable polymer materials is considered fundamental for efficient polymerisation to achieve satisfactory mechanical and physical properties (Andrade et al., 2016; Dressano et al., 2016; Randolph et al., 2014a; Randolph et al., 2016). Thus the differences in DC, KHN and flexural modulus reported in this investigation are likely to be related to the differences in photoinitiator properties and the efficiency for radical generation. For binary Type II systems that are

less efficient than Type I and ternary Type II systems, the lower DC and rates of polymerisation can be attributed to a fewer and slower generation of free radicals. From the steady-state (quasi-stationary) approximation, the rate of polymerisation is proportional to the concentration of radicals multiplied by the concentration of monomers (Andrzejewska, 2001). Since each MAPO and BAPO molecule generates either 2 or 4 radicals respectively through a more efficient photochemical process compared to a binary CQ sytems, which generate only one active radical through a less efficient process, the rate of polymerisation is expected to be greater in the former. However, for a ternary system, where back electron transfer is reduced, the rate of radical generation may be faster due to the availability of more excited CQ molecules, and the re-activation of inactive CQ molecules to produce more active radicals. Consequently it has been reported that ternary CQ systems can generate up to 4 active radicals per molecule of CQ (Cook and Chen, 2011; Ogliari et al., 2007). Thus whether radicals are generated using Type I initiators or ternary Type II systems, a higher number of radicals during polymerisation will lead to a multitude of growth centres, an earlier onset of autoacceleration and autodecelleration, and a more cross-linked polymer network compared to a slower generation of radicals that will lead to a more linear polymer network (Asmussen and Peutzfeldt, 2001a; Soh and Yap, 2004). Indeed, increased radical generation also increases the rate of termination, which is proportional to the squared concentration of radicals which may influence final DC. Nonetheless, the rate of polymerisation and final DC, regardless of polymer connectivity will be influenced by several factors including the rate and quantity of radical generation and the reaction temperature (Daronch et al., 2005; Randolph et al., 2014a). In the current investigation the rate of polymerisation was highest for the ternary Type II photoinitiator system at a concentration of 1mol% CQ system and was twice as high as binary CQ systems, but the highest conversion was achieved in the Type I BAPO based materials. Although BAPO and ternary CQ system both generate 4 active radicals per molecule, the higher polymerisation rate of the ternary CQ system is likely to vitrify the polymer quicker than BAPO materials resulting in a quicker onset of autodecceleration thus limiting DC. It is likely that this is controlled by reaction temperatures where ternary initiator systems is likely to have higher reaction exotherm than a system that is initiated by a unary process. Furthermore, despite the lower molar extinction coefficient, quantum yield efficiency and, generation of just one

free radical, the Type II CQ materials at a photoinitiator concentration of 1mol% was able to promote comparable DC compared to MAPO at 1mol% with the addition of iodonium salts.

Whilst DC is a useful indicator of reaction progress and polymer properties, it does not provide information on the polymer network structure, polydispersity of polymer chain lengths and extent of cross linking. Surface hardness prior to and following ethanol immersion has previously been used to indirectly assess polymer network formation and extent of cross linking (Asmussen and Peutzfeldt, 2001b; Benetti et al., 2009). Here, the lowest surface hardness was measured for the binary Type II CQ based masterials at a photoinitiator concentration of 0.5mol% resins followed by the Type I MAPO based system at a concentration of 0.5mol%..

After initial hardness, the specimens were immersed in ethanol during 24h. The results after ethanol immersion exhibited similar trends as the initial surface hardness measurements. It may be speculated that the differences between the groups could be related to the polymer formation. Ternary systems and the Type I initiator BAPO, which promoted the highest KHN (before and after ethanol immersion), generate 4 radicals to trigger the polymeric reation, which can generate more initiation centres, increasing significantly the rate of polymerization and consequently the crosslinking density of the polymer. Since the extent of softening in ethanol was similar for all materials irrespective of photoinitator type and concentration (~50% of the initial hardness value), it seems that the extent of cross-linking in each of the materials are comparable and mainly dependent on the resin matrix of the materials which was the same for each group in this study. However, the softening in ethanol has been used as an indirect way to measure the crosslinking density of polymers (Asmussen and Peutzfeldt, 1998, 2001a; Benetti et al., 2009), and slightly differences on the polymer formation probably could not be detected by this method, and may be responsible for the differences among the groups on KHN. Nevertheless, the differences were not relevant to influence the water sorption, solubility and flexural strength between the different photoinitiator systems. Notwithstanding, the difference observed for E, with the resins containing the Type I binary CQ photoinitiator at a concentration of 0.5mol% is likely to be related to the lower degree of conversion of the material.

Despite the reduced total absorbed energy per unit volume for CQ based systems, ternary CQ systems exhibit almost comparable efficiency as Type I initiators as reported in the current investigation, but may also have other advantages over Type I initiators particularly in deep curing

applications. For such applications, the short wavelengths of light that are needed to activate Type I initiators are firstly likely to scatter to a greater extent (Harlow et al., 2016), and secondly the high molar extinction coefficients are likely to reduce the spatial and temporal control of light transmission through depth. Coversely, for binary Type II CQ based systems, whilst longer can penetrate deeper into the materials, the lower efficiency of the photoinitiator limits DC and depth of cure. Indeed, although such problems are less problematic for thin adhesives layers, for deeper curing applications synergistic effects of Type I and Type II photoinitiators may address these limitiations . However, a ternary Type II based photoinitiator system represents an interesting approach conisidering issues associated with spectral, optical and spatial homogeneiety of modern multidiode multiwavelength LCUs.

5. Conclusions

The evaluation of novel photoinitiator systems that can address and optimise the limitiations of current photoinitiators in terms of curing efficiency (rate of polymerization, degree of conversion and depth of cure), aesthetics, chemico-physical properties and biocompatibility is important for material development. From this work, it appears that the potential to improve the rate of polymerization, degree of conversion and chemico-physical properties clearly depends on the photoinitiator system and its concentration. Despite the reduced total absorbed energy per unit volume for CQ based systems compared with Type I initiator systems, ternary Type II system (CQ, Amine and DPI) have the ability significantly improve the rate and degree of conversion compared to both Type I photoinitiators (MAPO and BAPO) and degree of conversion compared to MAPO only, whilst exhibiting comparable mechanical and physical properties compared to both Type I based materials. Such ternary photoinitiator systems may also have other advantages such as improved aesthetic and biocompatibility due to a lower concentration of pigmented photoinitiators and co-initiators as well as advantages for deeper/bulk curing applications which is of prime interest clinically. Further work is warrented on this topic.

References

Andrade, K.M., Palialol, A.R., Lancellotti, A.C., Aguiar, F.H., Watts, D.C., Goncalves, L.S., Lima, A.F., Marchi, G.M., 2016. Effect of diphenyliodonium hexafluorphosphate on resin cements containing different concentrations of ethyl 4-(dimethylamino)benzoate and 2-(dimethylamino)ethyl methacrylate as co-initiators. Dent Mater 32, 749-755.

Andrzejewska, E., 2001. Photopolymerization kinetics of multifunctional monomers. Prog Polym Sci 26, 605-665.

Asmussen, E., Peutzfeldt, A., 1998. Influence of UEDMA BisGMA and TEGDMA on selected mechanical properties of experimental resin composites. Dent Mater 14, 51-56.

Asmussen, E., Peutzfeldt, A., 2001a. Influence of pulse-delay curing on softening of polymer structures. J Dent Res 80, 1570-1573.

Asmussen, E., Peutzfeldt, A., 2001b. Influence of selected components on crosslink density in polymer structures. Eur J Oral Sci 109, 282-285.

Bacchi, A., Spazzin, A.O., de Oliveira, G.R., Pfeifer, C., Cesar, P.F., 2018. Resin cements formulated with thio-urethanes can strengthen porcelain and increase bond strength to ceramics. J Dent 73, 50-56.

Benetti, A.R., Asmussen, E., Munksgaard, E.C., Dewaele, M., Peutzfeldt, A., Leloup, G., Devaux, J., 2009. Softening and elution of monomers in ethanol. Dent Mater 25, 1007-1013.

Bertolo, M.V., Moraes, R.C., Pfeifer, C., Salgado, V.E., Correr, A.R., Schneider, L.F., 2017. Influence of Photoinitiator System on Physical-Chemical Properties of Experimental Self-Adhesive Composites. Braz Dent J 28, 35-39.

Chen, Y.C., Ferracane, J.L., Prahl, S.A., 2007. Quantum yield of conversion of the photoinitiator camphorquinone. Dent Mater 23, 655-664.

Cook, W.D., Chen, F., 2011. Enhanced photopolymerization of dimethacrylates with ketones, amines, and iodonium salts: the CQ system. J Polym Sci Part A: Polym Chem 49, 5030-5041.

Daronch, M., Rueggeberg, F.A., De Goes, M.F., 2005. Monomer conversion of pre-heated composite. J Dent Res 84, 663-667.

de Oliveira, D.C., Rocha, M.G., Gatti, A., Correr, A.B., Ferracane, J.L., Sinhoret, M.A., 2015. Effect of different photoinitiators and reducing agents on cure efficiency and color stability of resin-based composites using different LED wavelengths. J Dent 43, 1565-1572.

Dressano, D., Palialol, A.R., Xavier, T.A., Braga, R.R., Oxman, J.D., Watts, D.C., Marchi, G.M., Lima, A.F., 2016. Effect of diphenyliodonium hexafluorophosphate on the physical and chemical properties of ethanolic solvated resins containing camphorquinone and 1-phenyl-1,2-propanedione sensitizers as initiators. Dent Mater 32, 756-764.

Emami, N., Soderholm, K.J., 2005. Influence of light-curing procedures and photo-initiator/co-initiator composition on the degree of conversion of light-curing resins. J Mater Sci Mater Med 16, 47-52.

Ganster, B., Fischer, U.K., Moszner, N., Liska, R., 2008. New photocleavable structures. Diacylgermane-based photoinitiators for visible light curing. Macromolecules 41, 2394-2400.

Glickman, R.D., 2011. Ultraviolet phototoxicity to the retina. Eye Contact Lens 37, 196-205.

Goncalves, L.S., Moraes, R.R., Ogliari, F.A., Boaro, L., Braga, R.R., Consani, S., 2013. Improved polymerization efficiency of methacrylate-based cements containing an iodonium salt. Dent Mater 29, 1251-1255.

Guimaraes, T., Schneider, L.F., Braga, R.R., Pfeifer, C.S., 2014. Mapping camphorquinone consumption, conversion and mechanical properties in methacrylates with systematically varied CQ/amine compositions. Dent Mater 30, 1274-1279.

Guo, X., Wang, Y., Spencer, P., Ye, Q., Yao, X., 2008. Effects of water content and initiator composition on photopolymerization of a model BisGMA/HEMA resin. Dent Mater 24, 824-831.

Harlow, J.E., Rueggeberg, F.A., Labrie, D., Sullivan, B., Price, R.B., 2016. Transmission of violet and blue light through conventional (layered) and bulk cured resin-based composites. J Dent 53, 44-50.

Leprince, J.G., Hadis, M., Shortall, A.C., Ferracane, J.L., Devaux, J., Leloup, G., Palin, W.M., 2011. Photoinitiator type and applicability of exposure reciprocity law in filled and unfilled photoactive resins. Dental Materials 27, 157-164.

Meereis, C.T., Leal, F.B., Lima, G.S., de Carvalho, R.V., Piva, E., Ogliari, F.A., 2014. BAPO as an alternative photoinitiator for the radical polymerization of dental resins. Dent Mater 30, 945-953.

Nakamura, M., Yako, T., Kuse, Y., Inoue, Y., Nishinaka, A., Nakamura, S., Shimazawa, M., Hara, H., 2018. Exposure to excessive blue LED light damages retinal pigment epithelium and photoreceptors of pigmented mice. Exp Eye Res 177, 1-11.

Neumann, M.G., Miranda, W.G., Jr., Schmitt, C.C., Rueggeberg, F.A., Correa, I.C., 2005. Molar extinction coefficients and the photon absorption efficiency of dental photoinitiators and light curing units. J Dent 33, 525-532.

Neumann, M.G., Schmitt, C.C., Ferreira, G.C., Correa, I.C., 2006. The initiating radical yields and the efficiency of polymerization for various dental photoinitiators excited by different light curing units. Dent Mater 22, 576-584.

Ogliari, F.A., Ely, C., Petzhold, C.L., Demarco, F.F., Piva, E., 2007. Onium salt improves the polymerization kinetics in an experimental dental adhesive resin. Journal of Dentistry 35, 583-587.

Oxman, J.D., Jacobs, D.W., Trom, M.C., Sipani, V., Ficek, B., Scranton, A.B., 2005. Evaluation of initiator systems for controlled and sequentially curable free-radical/cationic hybrid photopolymerizations. J Polym Sci Pol Chem 43, 1747-1756.

Palin, W.M., Hadis, M.A., Leprince, J.G., Leloup, G., Boland, L., Fleming, G.J.P., Krastl, G., Watts, D.C., 2014. Reduced polymerization stress of MAPO-containing resin composites with increased curing speed, degree of conversion and mechanical properties. Dental Materials 30, 507-516.

Price, R.B., Labrie, D., Rueggeberg, F.A., Felix, C.M., 2010. Irradiance differences in the violet (405 nm) and blue (460 nm) spectral ranges among dental light-curing units. J Esthet Restor Dent 22, 363-377.

Randolph, L.D., Palin, W.M., Bebelman, S., Devaux, J., Gallez, B., Leloup, G., Leprince, J.G., 2014a. Ultra-fast light-curing resin composite with increased conversion and reduced monomer elution. Dental Materials 30, 594-604.

Randolph, L.D., Palin, W.M., Watts, D.C., Genet, M., Devaux, J., Leloup, G., Leprince, J.G., 2014b. The effect of ultra-fast photopolymerisation ofexperimental composites on shrinkage stress, network formation and pulpal temperature rise. Dental Materials 30, 1280-1289.

Randolph, L.D., Steinhaus, J., Moginger, B., Gallez, B., Stansbury, J., Palin, W.M., Leloup, G., Leprince, J.G., 2016. Photopolymerization of highly filled dimethacrylate-based composites using Type I or Type II photoinitiators and varying co-monomer ratios. Dent Mater 32, 136-148.

Schneider, L.F., Cavalcante, L.M., Prahl, S.A., Pfeifer, C.S., Ferracane, J.L., 2012a. Curing efficiency of dental resin composites formulated with camphorquinone or trimethylbenzoyl-diphenyl-phosphine oxide. Dent Mater 28, 392-397.

Schneider, L.F.J., Cavalcante, L.M., Prahl, S.A., Pfeifer, C.S., Ferracane, J.L., 2012b. Curing efficiency of dental resin composites formulated with camphorquinone or trimethylbenzoyl-diphenyl-phosphine oxide. Dental Materials 28, 392-397.

Soh, M.S., Yap, A.U., 2004. Influence of curing modes on crosslink density in polymer structures. J Dent 32, 321-326.

Timpe, H.J., Rajendran, A.G., 1991. Light-Induced Polymer and Polymerization Reactions .42. A Kinetic-Study of Cationic Photopolymerization with (Benzoin Derivative)/(Onium Salt) Systems. Eur Polym J 27, 77-83.

Figure Captions

Fig. 1 - Photoinitiator molar absorptivity and absolute irradiance of curing unit used

Fig. 2: The spectral absorbed energy per unit volume at equivalent molar concentrations (0.5mol%) for Type I photoinitiators, MAPO and BAPO, and the Type II photoinitiator, CQ. It can be seen that whilst the optical power of the Bluephase G2 light favours longer blue wavelenths (Figure 1), those wavelengths are weakly absorbed by the Type II photoinitiator, CQ, compared to the shorter violet wavelengths by Type 1 photoinitiators.

Fig. 3 – Real time degree of conversion (a) and rate of the polymerization (b) of groups tested.

Fig. 4 – Results obtained after microhardness evaluation (baseline) [a] and after ethanol immersion [b]. One-way ANOVA and Tukey's Test. Different letters indicate statistical difference. α=0.05.

Fig. 5 – Graphical representation of flexural modulus (a) and strength (b), water sorption (c) and solubility (d) of experimental groups. One-way ANOVA and Tukey's Test (flexural modulus and strength, water sorption). Medians e (interquartil-intervals 25%;75%) for solubility evaluation (Kruskal-Wallis, SNK). Different letters indicate statistical difference. α=0.05.