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New Role of Curcumin: as Multicolor Photoinitiator for Polymer Fabrication under Household UV to Red LED Bulbs

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Dedicated to Prof. Jun Nie on the occasion of his 50th birthday.

Curcumin exhibits broad ground state light absorption and can act as a photoinitiator for the free radical photopolymerization of methacrylates under air upon exposure to different household LED bulbs. The effects of temperature and various additives on the photoinitiation efficiency of curcumin-based systems have been investigated. The curcumin-based system exhibits the highest photoinitiation efficiency at 25°C. Additives also play an important role in the photoinitiation efficiency, and well-designed systems can even demonstrate higher efficiency than the commercial type I photoinitiator [phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide (XBPO)] and type II photoinitiator [camphorquinone (CQ)]. Interestingly, the curcumin/ diphenyliodonium hexafluorophosphate/triphenylphosphine combination is a capable multicolor photoinitiating system able to initiate free radical photopolymerization under air upon exposure to UV, blue, green, yellow, red, and warm white household LED bulbs. In addition, reversible addition-fragmentation chain transfer (RAFT) photopolymerization of *N*-isopropylacrylamide can also be achieved using curcumin-based system under irradiation of blue LED bulb. The photochemical mechanisms associated with the generation of radicals from the investigated photoinitiating systems are investigated by different techniques (fluorescence, steady state photolysis, and electron spin resonance spin-trapping methods) and discussed in detail. More interestingly, the polymer sample produced through photopolymerization process using curcumin-based photoinitiating system almost demonstrates no toxicity to human fibroblast Hs-27 cells endowing this photoinitiating system with great potential for fabrication of biocompatible polymeric materials.

Introduction

The design and development of visible-light-sensitive high-performance photoinitiators (PIs)^{1, 2} has been attracting increasing attention as the photochemical technique is one of the most promising approaches for the fabrication of various polymeric materials.³⁻⁹ Ultraviolet (UV) light has low penetration ability in photocurable formulations containing UV

absorbing compounds; visible light, on the other hand, can easily penetrate such formulations, and visible light photoinitiation is expected to be safer and more efficient than UV. Recent efforts have been devoted to the development of new compounds with novel chemical structures and excellent light absorption properties for use as visible light sensitive PIs.^{1,2} Among these, multicolor photoinitiators with panchromatic light absorption are extremely interesting, as they can utilize various wavelengths of incident light (from UV to red light) to initiate the polymerization of photocurable formulations despite containing other light absorbing compounds inside. However, very few multicolor photoinitiators have been reported, including 2,7-di-*tert*-butyldimethyldihydropyrene,¹⁰ indoline and squaraine dyes,¹¹ thiophene derivatives,¹² novel thioxanthone derivative,¹² indanedione derivative,¹³ thioxanthone derivative¹⁴ and the combination of different light absorbing perylene derivatives.¹⁵ The synthesis of these reported compounds is complicated, and they have been applied mainly in cationic or thiol-ene photopolymerizations. To the best of our knowledge, no natural dyes possessing panchromatic light absorption have been reported to act as multicolor photoinitiators.

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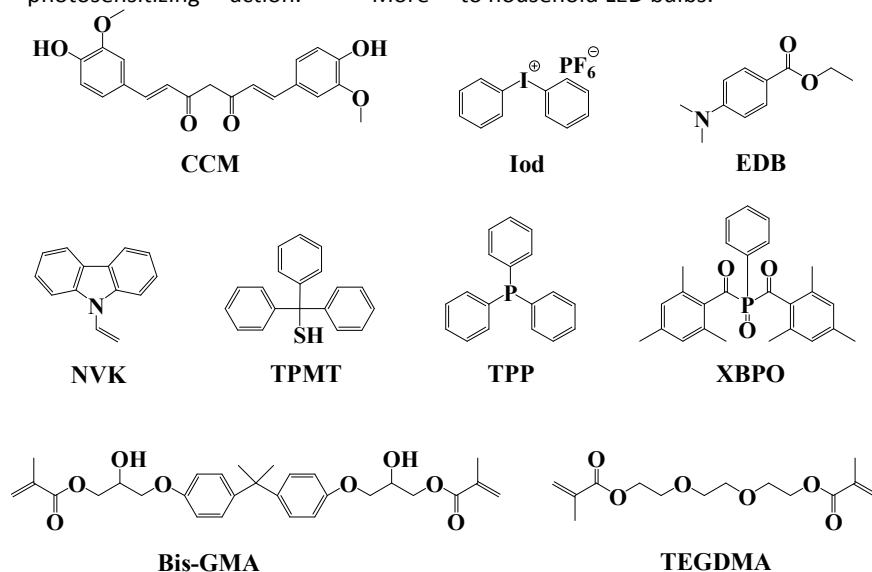
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Electronic Supplementary Information (ESI) available: [Emission spectrum of the warm white LED bulb (Figure S1); UV-vis absorption spectrum of CCM in Bis-GMA/TEGDMA blend (Figure S2); Photopolymerization profiles of Bis-GMA/TEGDMA blend at different temperatures under air in the presence of CCM/Iod upon UV LED exposure (Figure S3); Photopolymerization profiles of Bis-GMA/TEGDMA blend in the presence of CQ/EDB upon different LED exposure (Figure S4); Reversible addition-fragmentation chain transfer photopolymerization using CCM as photoinitiator (Figure S5); Photobleaching of Bis-GMA/TEGDMA blend in laminate in the presence of CCM/Iod upon UV LED exposure (Figure S6)]. See DOI: 10.1039/x0xx00000x

Curcumin (CCM, also known as turmeric) is a yellow-orange natural dye derived from the rhizomes of *Curcuma longa*, that has found widespread applications in fields ranging from pharmacology (e.g. anti-cancer, anti-bacterial, anti-inflammatory, and anti-oxidant applications)¹⁶⁻¹⁸ to photobiological and photosensitizing action.¹⁹⁻²¹ More

interestingly, it has also been reported that curcumin can act as a photoinitiator for cationic photopolymerization.^{22, 23} However, to the best of our knowledge, no detailed study has been reported of the use of CCM as a multicolor photoinitiator in free radical photopolymerization under air, upon exposure to household LED bulbs.



Scheme 1. Chemical structures of the investigated photoinitiators (CCM and XBPO), additives (Iod, EDB, NVK, TPMT and TPP) and monomers (Bis-GMA and TEGDMA).

In this work the ability of CCM, along with various additives, to photoinitiate free radical polymerization of Bisphenol A glycerolate dimethacrylate (Bis-GMA)/triethylene glycol dimethacrylate (TEGDMA) (70%/30%, wt%) blend (a typical dental resin system used here as benchmark monomer) under air is investigated. We utilize a series of household LED bulbs spanning a broad chromatic range – UV, blue, green, yellow, red, and warm white – as light sources. In addition, reversible addition-fragmentation chain transfer (RAFT) photopolymerization of *N*-isopropylacrylamide using curcumin-based system under irradiation of blue LED bulb is also studied. The photochemical mechanisms involved in the generation of radicals from the CCM-based photoinitiating systems (PISSs) are investigated and discussed in detail. Moreover, the cytotoxicity of the polymeric materials fabricated through the photopolymerization process using the curcumin-based photoinitiating system is also studied.

Experimental

Materials

The investigated curcumin (CCM), diphenyliodonium hexafluorophosphate (Iod), ethyl 4-(dimethylamino) benzoate (EDB), *N*-vinylcarbazole (NVK), triphenylmethanethiol (TPMT), triphenylphosphine (TPP), phenylbis(2,4,6-trimethylbenzoyl)phosphine oxide (XBPO), camphorquinone (CQ), and *N*-isopropylacrylamide (NIPAAm) were purchased from Sigma-Aldrich and used as received without further purification. Bisphenol A glycerolate dimethacrylate (Bis-GMA) and triethylene glycol dimethacrylate (TEGDMA) were also

obtained from Sigma-Aldrich, and the Bis-GMA/TEGDMA (70%/30%, wt%) blend was used as benchmark monomer for free radical photopolymerization. The chemical structures of the studied compounds are shown in Scheme 1.

Irradiation Sources

Different household LED bulbs were used as irradiation devices: UV LED (emission wavelength centered at 392 nm; incident light intensity: 100 mW cm⁻²), blue LED (455 nm; 100 mW cm⁻²), green LED (518 nm; 60 mW cm⁻²), yellow LED (594 nm; 30 mW cm⁻²), red LED (636 nm; 90 mW cm⁻²), and warm white LED (polychromatic light in the range of 410 - 750 nm; 100 mW cm⁻²); the emission spectrum was given in Figure S1 in the supporting information SI.

Photopolymerization Experiments

The photopolymerization reactions of Bis-GMA/TEGDMA blend in the presence of different curcumin-based photoinitiating systems were monitored using the photo-differential scanning calorimetry (photo-DSC): the DSC (Q20, TA instruments) equipped with household LED bulbs. For each measurement, approximately 5 mg of photocurable formulation was weighed and placed in a sample pan. And then the formulation was irradiated in the DSC apparatus in an isothermal condition under air atmosphere. The reaction heat at time *t* (ΔH_t) during the photopolymerization process was recorded continuously by DSC, and it was proportional to the amount of the reacted methacrylate double bonds of Bis-GMA/TEGDMA blend. Finally, the degree of double bond conversion *C* at time *t* was calculated from the equation: $C (\%) = (\Delta H_t/H_o) \times 100$ [where $H_o = 279 \text{ J/g}$ is the theoretical heat for 100% conversion of Bis-

GMA/TEGDMA blend, which is calculated on the basis of the enthalpy of polymerization (57.8 kJ/mol) for methacrylate double bonds²⁴].

Fluorescence Experiments

The fluorescence property of curcumin in acetonitrile was studied using the Cary Eclipse Fluorescence Spectrophotometer (Agilent Technologies). The interaction rate constants k_q between curcumin and additives (*i.e.* Iod or EDB) were extracted from the classical Stern-Volmer treatment²⁵ ($I_0/I = 1 + k_q\tau_0[\text{additive}]$; where I_0 and I stand for the fluorescent intensity of curcumin in the absence and the presence of the additives, respectively; τ_0 stands for the lifetime of curcumin in the absence of additives).

Steady State Photolysis Experiments

Curcumin in the presence of additives (*i.e.* Iod or EDB) in acetonitrile were irradiated with the UV LED bulb, and the UV-vis spectra were recorded using the Cary 300 UV-VIS Spectrophotometer at different irradiation time.

ESR Spin Trapping (ESR-ST) Experiments

ESR-ST experiments were carried out using the Bruker EMX-plus X-Band ESR Spectrometer. The radicals were generated at room temperature upon the UV LED exposure under argon and trapped by phenyl-*N-tert*-butylnitron (PBN) according to a procedure²⁶ described elsewhere in detail. The ESR spectra simulations were carried out with the WINSIM software.

In vitro cell culture

Human fibroblast Hs-27 cells were obtained from European Collection of Cell Cultures (ECACC). Hs-27 cells were cultured in T25 cell culture flask with 5% CO₂ at 37 °C. The culture medium was composed of Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% fetal bovine serum, 100 U/mL penicillin, 100 µg/mL streptomycin and 1× GlutaMAX™. After the cells reached confluence, the cells were washed with phosphate buffered saline (PBS) and detached by trypsin/EDTA treatment. The cells were collected, centrifuged and resuspended in culture medium for the further experiments.

Cytotoxicity in a contact model

10 mg of Bis-GMA/TEGDMA (70%/30%, wt%) blend containing CCM/Iod (0.5%/2%, wt%) photoinitiating system was dropped into 96-well cell culture plates and then polymerized under air upon exposure to the UV LED. After being washed with 70% ethanol for 2 h, Hs-27 suspension was seeded in 96-well cell culture plates at 8,000 cells per well and cultured with 200 µL medium at 37 °C for 3 days. The cell viability was measured using a WST-1 assay (Roche Diagnostics). This is a colorimetric assay for the quantification of cell viability and proliferation that is based on the cleavage of a tetrazolium salt (WST-1) by mitochondrial dehydrogenases in viable cells. Increased enzyme activity leads to an increase in the amount of formazan dye, which is measured with a microplate reader. After incubation for 3 days, 20 µL WST-1 was added into the cell culture medium. The plates were then incubated for an

additional 2 hours at 37 °C. After incubation, 100 µL of solution was taken out in a new 96-well plate and the absorbance of the samples against the background control on a Benchmark Microplate Reader (Bio-Rad) was obtained at a wavelength of 440 nm with a reference wavelength of 650 nm. All cytotoxicity data are reported as mean ± standard deviation.

Cytotoxicity in a non-contact model

Hs-27 suspension was seeded in a 24-well cell culture plate at 100,000 cells per well and cultured with 2 mL medium at 37 °C for 1 day. 125 mg of polymer was prepared from the photopolymerization of Bis-GMA/TEGDMA (70%/30%, wt%) blend initiated by CCM/Iod (0.5%/2%, wt) photoinitiating system under the UV LED irradiation. After being washed with 70% ethanol for 1 day, the polymer block was placed in a well insert (membrane pore = 8.0 µm) and immersed in the well with cells. The cells were culture for another 7 days and the medium was exchanged once during the culture. The cell viability was also measured with the WST-1 assay. The culture medium and well inserts were removed and 500 µL fresh medium was added along with 50 µL WST-1 to each well. The plates were then incubated for an additional 2 hours at 37 °C. After incubation, 200 µL of solution was taken out in a new 96-well plate and the absorbance of the samples against the background control was obtained at a wavelength of 440 nm on the Benchmark Microplate. All cytotoxicity data are reported as mean ± standard deviation.

Results and discussion

Light Absorption Property of Curcumin

The absorption spectrum of CCM in acetonitrile is shown in Figure 1 (a). As illustrated, CCM exhibits an intense light absorption maximum (λ_{max}) at 417 nm ($\epsilon_{\text{max}} = 58500 \text{ M}^{-1} \text{ cm}^{-1}$) which can be assigned to $\pi\text{-}\pi^*$ transitions.²⁰ The red edge of the CCM absorption spectrum ($\lambda > 500 \text{ nm}$) was measured at a higher concentration in acetonitrile [Figure 1 (b)] (a similar spectrum has been reported previously²⁷). Similarly, in Bis-GMA/TEGDMA (70%/30%, wt%) blend (CCM concentration = 0.5 wt%), a significant broad light absorption feature, which extends to 650 nm is also observed (Figure S2 in the SI). Interestingly, the panchromatic absorption spectrum of curcumin exhibits overlapping with the emission spectra of various household LED bulbs [Figure 1 (b)], which endows it with the potential to act as a multicolor photoinitiator.

Photoinitiating Ability of Curcumin for Free Radical Photopolymerization of Methacrylates

Effect of different temperature. Free radical photopolymerization of a Bis-GMA/TEGDMA blend in the presence of CCM/Iod system under air was carried out using a UV LED bulb. As demonstrated in Figure S3 in the SI, the photopolymerization rate and the final conversion increases with temperature. Specifically, after 300 s of UV LED irradiation, the polymerization conversion of the Bis-GMA/TEGDMA blend was 36%, 38% and 58%

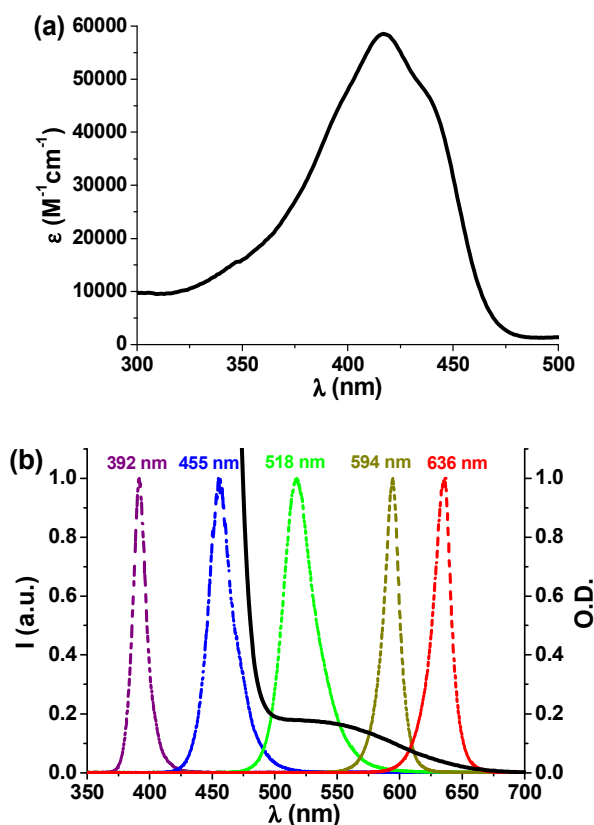


Figure 1. (a) UV-Vis absorption spectrum of CCM in acetonitrile; (b) Emission spectra of UV (392 nm), blue (455 nm), green (518 nm), yellow (594 nm) and red (636 nm) LED bulbs, and their overlap with the absorption spectrum of CCM.

at 0, 10 and 25°C, respectively. The lower polymerization rates and conversions at the lower temperatures can be ascribed to the decreased mobility of the generated radicals.²⁸ At 50°C, the highest temperature used in this work, the photopolymerization of Bis-GMA/TEGDMA blend could not be accurately determined using photo-DSC. This was due to the oxygen inhibition effect becoming much more significant owing to the decreased viscosity of the formulation at the higher temperature and no polymerization reaction occurred in this situation.

Effect of various additives. Various additives (Scheme 1) in combination with curcumin were used as photoinitiating systems for free radical polymerization of a Bis-GMA/TEGDMA blend at 25°C under air using the UV LED bulb. Iod is a well-known photoinitiator but can only work under < 300 nm UV irradiation.²⁵ It was selected here as an additive in the CCM-based photoinitiating system because it may be photosensitized by CCM to generate radicals for polymerization under irradiation by a longer wavelength. As illustrated in Figure 2 and Table 1, a two-component PIS consisting of CCM and Iod initiated methacrylate polymerization with a final conversion of 58% (UV LED at 392 nm), which was similar to that of the well-known commercial photoinitiator XBPO (56%). The other two-component PIS tested, which consisted of CCM and EDB (a tertiary amine, usually used as a coinitiator with type II

photoinitiators), exhibited a lower photopolymerization rate and conversion for polymerization of the same Bis-GMA/TEGDMA formulation than those of XBPO.

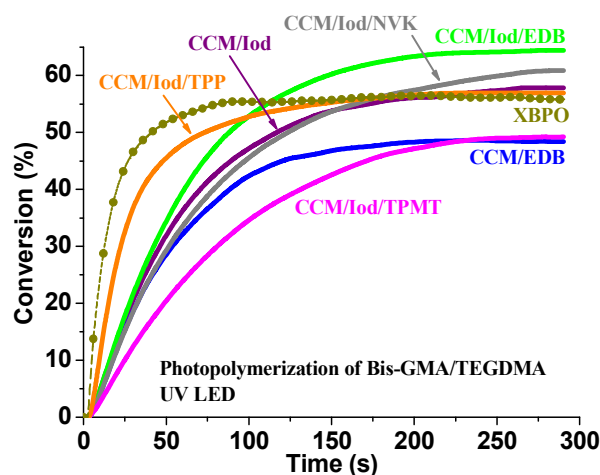


Figure 2. Photopolymerization profiles of Bis-GMA/TEGDMA (70%/30%, wt%) blend at 25°C under air in the presence of CCM/additive1/ (additive2) (0.5%/2%/2%, wt%) upon UV LED exposure. XBPO (0.5 wt%), used as a reference, is shown as a dashed line.

Even though the two-component photoinitiating systems can initiate the radical photopolymerization, the effect of an additional additive was also studied. Improved photoinitiation efficiency can be expected with a suitable second additive. Of the three-component systems investigated, CCM/Iod/EDB was more efficient than the two-component PISs, and produced a higher final conversion (64%) for the methacrylates than XBPO. But the polymerization rate of the CCM/Iod/EDB PIS was still much lower than XBPO. The addition of a second additive to the CCM/Iod system also influenced the photoinitiation ability: adding TPMT significantly diminished the polymerization efficiency of the system probably due to the degradation of CCM or Iod by TPMT, while the addition of NVK slightly increased the final conversion of methacrylates. The addition of TPP markedly increased the efficiency of the PIS (CCM/Iod /TPP PIS) due to the ability of TPP to overcome oxygen inhibition.^{29, 30} The polymerization rate for this system was accordingly the highest among all the investigated CCM-based systems, while the polymerization rate and final conversion were comparable with those of XBPO.

Effect of diverse irradiation devices (LED bulbs). As shown in Figures 1 (b) and S2 in the SI, the panchromatic absorption of curcumin endows it with the potential to act as a multicolor photoinitiator. The three-component photoinitiating system, CCM/Iod/TPP, at 25°C, was selected here for investigation as this system presented the highest efficiency among all the studied CCM-based PISs under UV LED exposure (Figure 2). As illustrated in Figure 3 and Table 1, the CCM/Iod/TPP combination initiated polymerization of the Bis-GMA/TEGDMA blend under exposure to all LED bulbs (i.e. UV to red LED bulbs, and the warm white LED bulb). The final methacrylates conversions upon exposure to the UV green or warm white LED bulb were similar to that of the XBPO

Table 1. Photopolymerization conversions of Bis-GMA/TEGDMA (70%/30%, wt%) blend obtained at 25°C under air upon exposure to LED bulbs for 300 s in the presence of CCM/additive1/additive2 (0.5%/2%/2%, wt%); XBPO (0.5 wt%) and CQ/EDB (0.5%/2%, wt%) as references.

PISs	UV LED	Blue LED	Green LED	Yellow LED	Red LED	Warm white LED
CCM/Iod	58%					
CCM/EDB	48%					
CCM/Iod/EDB	64%					
CCM/Iod/TPMT	49%					
CCM/Iod/NVK	61%					
CCM/Iod/TPP	57%	71%	54%	38%	34%	56%
XBPO	56%	28%	np	np	np	
CQ/EDB	35%	61%	27%	np	np	

np: no polymerization

system under the UV LED (~50%). Remarkably, curcumin-based CCM/Iod/TPP PIS demonstrated a methacrylate photopolymerization efficiency of 71% when the blue LED bulb was used. The photopolymerization efficiency for XBPO under the same exposure conditions was much lower (28%). The Bis-GMA/TEGDMA blend was also photopolymerized under irradiation by the yellow and red LEDs. At these longer wavelengths the efficiency was lower (methacrylates conversion = 38% and 34% for yellow LED and red LED, respectively), but the XBPO PI yielded no polymerization at these wavelengths. More interestingly, CCM/Iod/TPP system also demonstrated higher efficiency than the well-known visible-light-sensitive type II photoinitiating system camphorquinone (CQ)/EDB upon exposure to UV, blue, and green LED bulbs (Table 1 and Figure S4 in the SI).

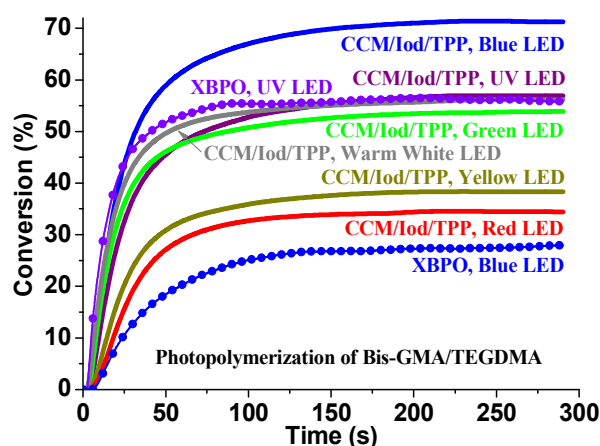


Figure 3. Photopolymerization profiles of Bis-GMA/TEGDMA blend (70%/30%, wt%) at 25°C under air in the presence of CCM/Iod/TPP (0.5%/2%/2%, wt%) upon different LED exposure; XBPO (0.5 wt%) as a reference shown with dashed lines.

More interestingly, the CCM/Iod/TPP-based formulation can also be photocured under ambient sunlight within 10 min, indicating the high performance of the CCM/Iod/TPP system. As a result, it can be seen clearly that the photopolymerization efficiency under different LED bulbs were related to i) the extent of the overlapping between the light absorption of CCM and the emission wavelength of the LED bulbs, ii) the incident light intensity of the LED bulbs (see in the Experimental Section, Irradiation Sources), and iii) the penetration of incident light into the formulations. All three factors affect the photopolymerization efficiency.

In addition to cross-linked photopolymerization of multifunctional methacrylate (Bis-GMA/TEGDMA blend), CCM can also act as photoinitiator for reversible addition-fragmentation chain transfer (RAFT) photopolymerization of *N*-isopropylacrylamide (NIPAAm) under the irradiation of blue LED bulb and PNIPAAm ($M_n = 43500$ g/mol) with low polydispersity (PDI = 1.12) can be obtained after 150 minutes of light irradiation (Figure S5 in the SI).

Photochemical Mechanisms: Generation of Radicals in the Curcumin-based PISs. The photophysical and photochemical properties of curcumin itself have been widely investigated.^{19, 20, 31-33} This research is instead concerned with mechanisms for the generation of radicals in the CCM-based PISs.

Table 2. Parameters calculating the free energy changes (ΔG) for the electron transfer between curcumin and additive.

	E_{ox} (V vs. SCE)	E_{red} (V vs. SCE)	E_s (eV) ^e	ΔG_s (eV) ^f	E_T (eV) ^g	ΔG_T (eV) ^h
Curcumin/Iod	0.55 ^a	-0.2 ^c	2.68	-1.93	1.98	-1.23
Curcumin/EDB	1.0 ^b	-1.2 ^d	2.68	-0.48	1.98	0.22

^a oxidation potential of curcumin;¹⁸ ^b oxidation potential of EDB;³⁵ ^c reduction potential of Iod;¹ ^d reduction potential of curcumin;^{36,37} ^e singlet state energy of curcumin extracted from the UV-vis absorption and fluorescence emission spectra of curcumin as usually done;³⁸ ^{f or h} ΔG = free energy change for the curcumin/additive (Iod or EDB) singlet (ΔG_s) or triplet state (ΔG_T) interaction; ^g triplet state energy of curcumin.³⁹

Following light absorption, the fluorescence emission of CCM in acetonitrile (fluorescence lifetime, $\tau_0 \sim 376 - 695$ ps; fluorescence quantum yield, $\Phi_f \sim 0.1$)²⁰ is from the first excited singlet state. In the presence of Iod or EDB, however, CCM fluorescence is quenched by electron transfer reactions ($k_q \tau_0 = 10.46$ and 10.12 for CCM/Iod and CCM/EDB, respectively). The large interaction rate constants ($k_q \sim 10^{10} \text{ M}^{-1} \text{ s}^{-1}$) for CCM/additive indicate that the processes are almost diffusion-controlled. In addition, the free energy change, ΔG_S for electron transfer between singlet-excited CCM and the additive (Iod or EDB) can be calculated from the classical Rehm-Weller equation:³⁴ $\Delta G = E_{\text{ox}} - E_{\text{red}} - E_S + C$; where E_{ox} , E_{red} , E_S , and C are the oxidation potentials of the electron donor, the reduction potential of the electron acceptor, the excited singlet state energy of curcumin, and the electrostatic interaction energy for the initially-formed ion pair, which is generally considered to be negligible in polar solvents. As summarized in Table 2, the negative values of the free energy changes ΔG_S for the CCM/Iod (-1.93 eV) or CCM/EDB (-0.48 eV) electron transfer reactions ensure the favorability of the processes.

The singlet-excited CCM can also undergo intersystem crossing to an excited triplet state ($\Phi_T \sim 0.11$, $\tau_T \sim 2.48 \mu\text{s}$)¹⁹. The triplet route in the CCM/Iod interaction cannot be ruled out as the process is energetically favorable (Table S2, $\Delta G_T < 0$). On the other hand, there was no excited triplet state involved in the CCM/EDB interaction as the relevant $\Delta G_T > 0$.

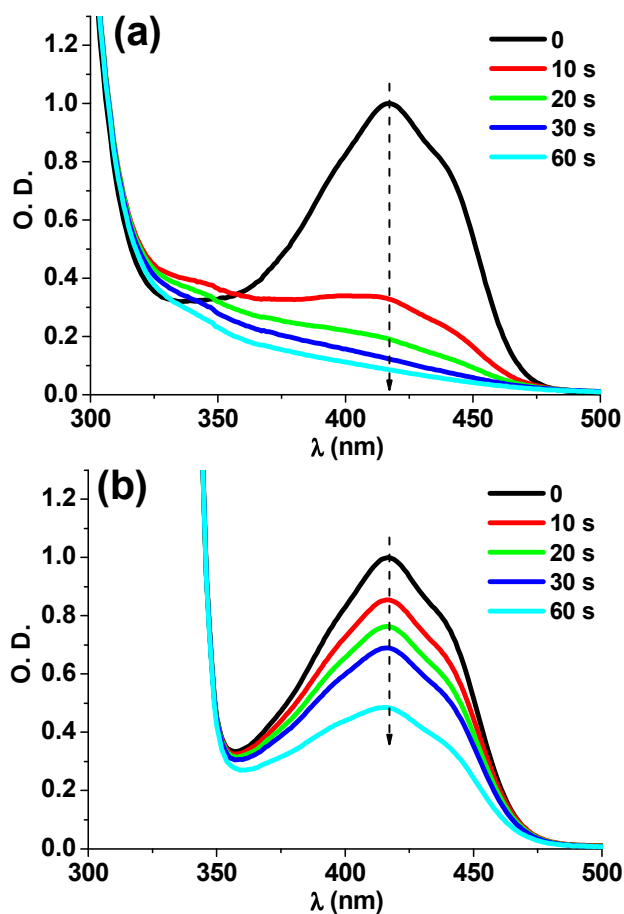


Figure 4. Steady state photolysis of (a) CCM/Iod and (b) CCM/EDB in acetonitrile upon UV LED exposure ([Iod] = 7.5 mM; [EDB] = 15.0 mM); indicated by UV-vis spectra recorded at the indicated irradiation times.

The photochemical reactivity between CCM and additives (Iod or EDB) was investigated by steady state photolysis experiments. As shown in Figure 4, the ground state absorption of the CCM/Iod system [Figure 4 (a)] in acetonitrile rapidly decreased during UV LED irradiation. Dramatic photobleaching was observed after only 1 minute of irradiation, which indicated the high reactivity of this system. In addition, the excellent photobleaching properties of the system endow it with the potential for use in the fabrication of colorless materials (the photobleaching in CCM/Iod can also be observed in the Bis-GMA/TEGDMA formulation during the photopolymerization reaction, Figure S6 in the SI). In contrast, the photobleaching of CCM/EDB was relatively slow [Figure 4 (b)], which can be ascribed to the relatively lower reactivity of this system. This result is in agreement with the greater photoinitiation ability of CCM/Iod PIS for the FRP of Bis-GMA/TEGDMA (Figure 2).

Following electron transfer in the CCM/Iod and CCM/EDB systems under light irradiation, the generated radicals can be observed directly by ESR spin trapping experiments (Figure 5). The hyperfine splitting constants (HFS) for both the nitrogen (a_N) and the hydrogen (a_H) of the PBN/radical adducts can be used to determine the specific radicals. In the CCM/Iod system $a_N = 14.3$ G and $a_H = 2.2$ G were measured, leading to the assignment of PBN/phenyl radical adducts,^{40, 41} while $a_N = 14.3$ G and $a_H = 2.4$ G for the CCM/EDB system were assigned to PBN/aminoalkyl radical adducts.^{42, 43} It is well known that curcumin can act as a free radical scavenger,⁴⁴ but its role as a photoinitiator (but not a free radical scavenger) predominates in the relevant photoinitiating systems based on the ESR results.

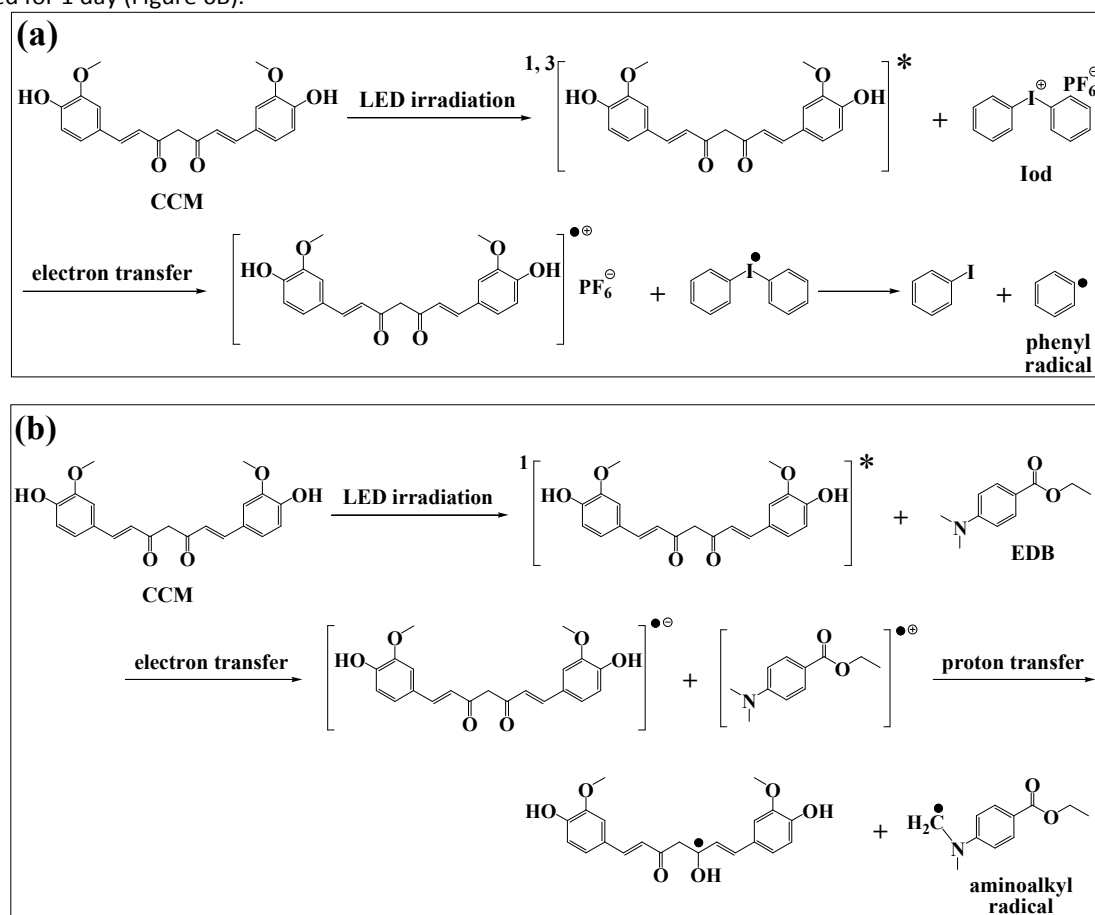
Based on the above investigation, phenyl radicals and aminoalkyl radicals can be generated in the CCM/Iod and CCM/EDB systems respectively during LED irradiation, through the photochemical mechanisms presented in Scheme 1. In CCM/Iod/additive2 systems, new radicals can also be produced to initiate photopolymerization.^{29, 45}

Cytotoxicity of Polymers Fabricated through Photopolymerization using Curcumin-based Photoinitiating system. The cytotoxicity of polymers is normally dependent on i) type of end group that has been imparted onto the polymers during the photoinitiation process (e.g. phenyl group for CCM/Iod system in this study; it is also confirmed by the HNMR of the polymer prepared from the photopolymerization of di(ethylene glycol) methyl ether methacrylate using CCM/Iod photoinitiating system under blue LED irradiation); ii) type of monomers (e.g. in this study, the typical dental resin system Bis-GMA/TEGDMA was used as benchmark monomer); and iii) the amount and cytotoxicity of residual photoinitiating components (and their photoreacted products) left in the polymers. In this study, polymeric materials were prepared from the photopolymerization of Bis-GMA/TEGDMA (70%/30%, wt%) blend initiated by CCM/Iod (0.5%/2%, wt%) photoinitiating system under the UV LED irradiation. The

cytotoxicity of polymers was tested in both a contact model and a non-contact model with human fibroblast Hs-27 cells.

In the contact model for cytotoxicity test, Hs-27 cells were seeded directly onto the washed polymers (with 70% ethanol) and incubated for 3 days. After culture for 3 days, the results from a WST-1 based cell viability assay revealed that the cell proliferation was inhibited in contact with the sample (Figure 6A). The reason might be related to weak cell attachment of the electric neutrality of the polymers: compared with the control (Figure 6C), less cells adhere on the samples after being seeded for 1 day (Figure 6B).

However, the polymers almost showed no toxicity to Hs-27 cells in the non-contact model (Figure 7A). In Figure 7B, the viability of Hs-27 cells was very close to the controls (94.5%). There was no obvious difference in the cell morphology between the sample group and the control group (Figures 7C and 7D). It revealed that the end group imparted onto the polymers and the residual photoinitiating components (and their photoreacted products) exhibited no toxicity, and the non-toxicity property of the polymers indicates that the curcumin-



Scheme 1. Photochemical mechanisms on the generation of radicals in (a) CCM/Iod and (b) CCM/EDB.

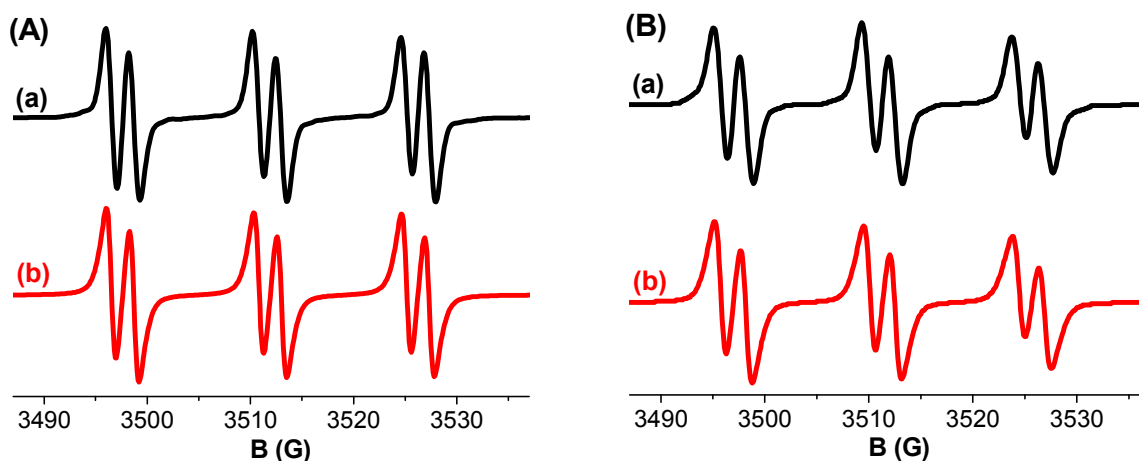


Figure 5. ESR spectra of radicals generated in (A) CCM/Iod and (B) CCM/EDB upon UV LED exposure and trapped by PBN in tert-butylbenzene: (a) experimental and (b) simulated spectra.

based photoinitiating system has great potential for the fabrication of biocompatible polymeric materials. More investigation on the correlations between different photoinitiating systems (and monomers) and cytotoxicity of related produced polymers is very interesting and will be carried out using different approaches such as mass spectrometry⁴⁶⁻⁴⁸ in the forthcoming papers.

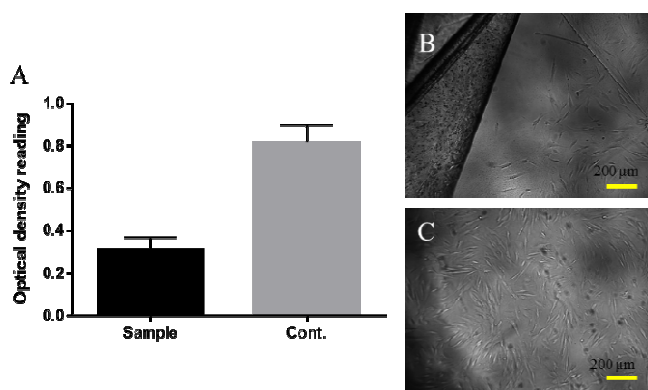


Figure 6. Contact cytotoxicity test of sample with HS-27 cells cultured in 96 well microplates. A. Optical density reading of WST-1 assay. B&C, Photomicrographs of HS-27 cells with the sample and without the sample, respectively. Scale bars = 200 μm.

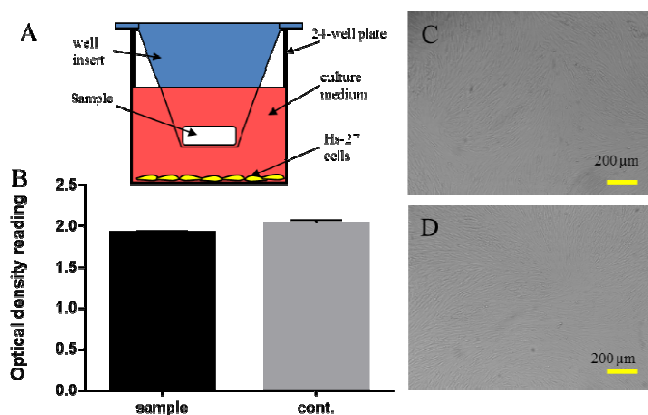


Figure 7. Non-contact cytotoxicity test of sample with HS-27 cells cultured in 24 well microplates. A Scheme of the cell culture model. B. Optical density reading of WST-1 assay. C&D, Photomicrographs of HS-27 cells with the sample and without the sample, respectively. Scale bars = 200 μm.

Conclusions

To summarize, this research revealed that curcumin in combination with suitable additives can initiate free radical photopolymerization with high photoinitiation efficiency during irradiation by household LED bulbs. The curcumin-based photoinitiating system demonstrated the highest photopolymerization efficiency when carried out at 25°C. Moreover, the curcumin/iodonium salt/triphenylphosphine system could initiate the photopolymerization of methacrylate under air upon exposure to UV, blue, green, yellow, red, and

warm white household LED bulbs, thus giving it panchromatic photoinitiation ability. In addition, the curcumin/iodonium salt/triphenylphosphine combination was more efficient for the radical photopolymerization of methacrylate than the commercial type I photoinitiator XBPO and type II photoinitiating system CQ/EDB under irradiation by UV to red LED bulbs. Furthermore, curcumin-based system can also initiate RAFT photopolymerization of NIPAAm to produce PNIPAAm (Mn = 43500 g/mol) with low PDI (1.12) under irradiation of blue LED bulb. The mechanism studies demonstrated that phenyl radicals and aminoalkyl radicals can be generated in the curcumin/iodonium salt and curcumin/amine systems during LED irradiation through electron transfer reactions, and that new radicals can also be produced to initiate the photopolymerization if another additive is included in the systems. More interestingly, the polymers produced through the photopolymerization process using the curcumin-based photoinitiating system almost demonstrated no toxicity to human fibroblast Hs-27 cells. This research is expected to pave the way for the application of curcumin-based photoinitiating systems in the fabrication of biocompatible polymeric materials.

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Notes and references

The authors declare no competing financial interest.

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