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Full Paper

## A green approach to crosslinked polymer microspheres with undoped methacrylate monomers and their potential application as dental restorative materials

Xiangling Gu,<sup>a</sup> Xinfeng Song,<sup>a</sup> Yancong Zhang,<sup>a</sup> Hanwen Sun,<sup>\*a</sup> Xiang Zheng Kong,<sup>\*b</sup> Chunhua Fu,<sup>a</sup> Shuqin Cui<sup>a</sup> and Zhiqin Zhang<sup>a</sup>

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Herein, a green approach to crosslinked polymer microspheres with undoped methacrylate monomers is presented. The protocol is set up by means of photoinitiated precipitation polymerization of trifunctional crosslinker, i.e. trihydroxymethyl propane trimethyl acrylate (TMPTMA) and methyl methacrylate (MMA) for the purpose of achieving pure and crosslinked microspheres. The evolution of photoinitiated precipitation polymerization is tracked and the formation mechanism of poly (TMPTMA-MMA) microspheres is also elucidated. Finally, the potency of so-obtained crosslinked microspheres are explored to serve as organic fillers in dental restorative materials.

### Introduction

Polymer microspheres based on methacrylate monomer are known as one of the most widely used biomedical materials. A large number of the potential applications, such as drug delivery, wound dressing, tissue engineering, biological separation and dental restoration, are envisaged from such microspheres.<sup>1-6</sup> In the area of dental materials, poly(methyl methacrylate) (PMMA) microspheres are used as one of the main ingredients of composite resin, namely a kind of particle reinforced composite material based on PMMA, usually composed of a heterogeneous mixture including organic resin and inorganic filler.<sup>7,8</sup> Among them, the inorganic phase is usually of powdery inorganic fillers achieved by special surface treatment, commonly dispersed in the resin matrix in order to enhance its strength and modulus. As for the organic phase, it is mainly composed of resin matrix, monomer and photoinitiator. The resin matrix is mostly of methacrylate based polymer, formed by the curing process via a radical polymerization. The composite resin is largely used as dental restorative material, for their desirable colour and lustre, high mechanical strength and wear resistance and low thermal expansivity. It was formerly used for the restorative material of anterior teeth, but, recently, it further replaced the silver amalgam in defect restoration of posterior teeth.<sup>9,10</sup>

Compared with the silver amalgam, the abrasion performance of organic resin needs to be improved. The present measure to this end is adding a large amount of inorganic filler, such as silicon dioxide and zirconium dioxide, into the organic phase.<sup>11</sup> However, the use of inorganic filler often brings about a few problems. For one thing, the inorganic filler should be subjected to complex treatment, for example, silanization, with

the purpose of improving its adhesive strength to the resin matrix; In the next place, the hardness of inorganic filler is much higher than that of the tooth itself, which causes excessive wearout or damage in the process of chewing. Last but not least, the adhesive strength between inorganic fillers and resin matrix tends to decline at a speed of geometric level over time especially in the complex oral environment of human body, and the abrasion resistance of such composite resin degrades dramatically. In recent years, organic fillers are gradually taken into account to replace inorganic fillers.<sup>12,13</sup> The chemical bonds formed between organic filler and resin matrix are more robust than the cohesive strength between inorganic fillers and resin matrix. Furthermore, the chemical bonds decline at a very slow speed and the hardness of organic fillers can be adjusted in a certain scope to keep consistent with that of various kinds of teeth. Therefore, adding organic filler into resin matrix is becoming an effective way to solve the problems resulted from the use of inorganic fillers.

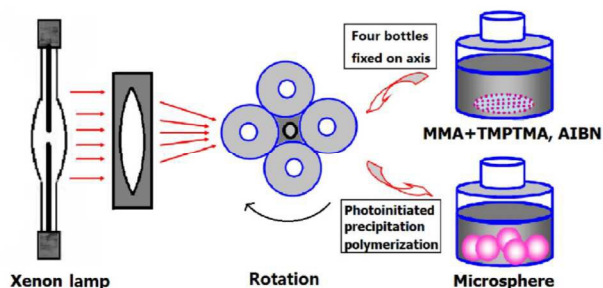
Recently, *Homo-* or *co-*PMMA microspheres were preliminarily used as organic fillers in dental materials where highly precise microspheres structures were needed.<sup>7,8</sup> PMMA is one of the most widely accepted biomaterial in prosthetic dentistry due to its well-known advantages.<sup>14</sup> However these materials are far from being ideal because of the micro-effusion from volumetric shrinkage of the in-situ formed composite resin and the inferior mechanical performance, such as the hardness. To this end, the present study focused in seeking a kind of desirable PMMA microsphere to serve as the organic filler in dental restorative material, which should have little volumetric shrinkage and appropriate mechanical properties with an ease to

meet the demand of dental material.

As is known that many classical polymerization methods, including dispersion polymerization,<sup>15-18</sup> emulsion polymerization,<sup>19,20</sup> suspension polymerization<sup>21,22</sup>, were adopted for the sake of preparing *homo*- or *co*-PMMA microspheres. Furthermore, a few unconventional tools, for example, electrospray,<sup>23</sup> micro-porous glass membrane emulsification,<sup>24</sup> and microfluidic emulsification<sup>25</sup> have also been employed to develop novel ways of the preparation of PMMA microspheres. It is beyond all doubt that those studies contributed largely to the research of PMMA microspheres, but most of them could not be carried out without the use of surfactants or stabilizers, because they need to avoid the coalescence of microspheres. However, the application of such microspheres in prosthetic dentistry was limited due to the negative effects of those redundant agents on colour, lustre and transparency.<sup>26</sup> Although all or most of those reagents could be removed by repeated washing after the polymerization, the process was too tedious and costly for further application. In addition, the preparation through these way were usually carried out with harsh conditions, for example, toxic organic solvents,<sup>23,27,28</sup> high temperature<sup>19,29</sup> and high pressure.<sup>30,31</sup> Therefore, it is essential to explore a green approach to achieve pure PMMA microspheres at mild conditions.

Precipitation polymerization has been introduced to prepare polymer microspheres free of surfactants or stabilizers in recent years. It was firstly performed with divinylbenzene (DVB) or ethyleneglycol dimethacrylate (EGDMA) as crosslinkers *via* a thermal-initiated manner.<sup>32,33</sup> Co or UV irradiation has also been adopted to trigger the polymerization for ambient temperature synthesis of monodisperse microspheres by Naka *et al*,<sup>34</sup> Barner *et al*<sup>35</sup> and Limé *et al*<sup>36</sup>. In those polymerizations, PMMA microspheres were still prepared in toxic solvents, such as tetrahydrofuran, toluene and acetonitrile. What is more, microsphere yields in those polymerization were usually limited to a level lower than 50%, which was considered as a result of the use of difunctional crosslinkers, namely DVB and EGDMA.

In order to achieve pure PMMA microsphere for the application in dental restorative materials, we developed a green approach to polymer microspheres by photoinitiated precipitation polymerization of trihydroxymethyl propane trimethyl acrylate (TMPTMA, the crosslinker) and MMA in low-toxicity solvent-ethanol. Compared with the previous reports, this work has three novelties as follows: Firstly, microsphere yield of poly (TMPTMA-MMA) was improved to a level higher than 90% by the use of designed amount of trifunctional crosslinker of TMPTMA. Secondly, to the best of our knowledge, the attempt of applying poly (TMPTMA-MMA) microspheres with undoped methacrylate monomer as organic filler of dental materials, has never been reported previously, although similar polymerization technology was developed by other researchers. Because another component in dental restorative materials, namely the resin matrix, was commonly synthesized with methacrylate monomer, the compatibility between the organic filler and the resin matrix could be improved through this way. We think this may be one of the key reasons for the decrease of volumetric shrinkage of as-prepared dental restorative materials. Thirdly, up to now,



**Scheme 1** Illustration of the formation of microspheres *via* photoinitiated precipitation polymerization of TMPTMA and MMA with AIBN as initiator.

the hardness of inorganic fillers added in dental restorative materials was difficult to match with the human tooth itself, because the inorganic materials often had high, unadjustable hardness. Facing this challenge, the so-obtained poly (TMPTMA-MMA) microspheres were employed as organic fillers with adjustable and controllable hardness. Though crosslinking is often considered as a routine technique to change the hardness of polymer products, the use of crosslinked polymer microspheres in dental restorative materials to adjust the hardness was reported herein for the first time, and may open up a novel way for the preparation of dental restorative materials.

## Experimental

### Preparation of poly (TMPTMA-MMA) microspheres

Polymerizations were carried out in sets of 2-6 parallel experiments using clean and screw-cap quartz glass bottles of 120 mL. In a typical polymerization, each bottle was charged with a same amount (2 mL) of monomers of TMPTMA (industrial grade, Tianjiao Chemicals, Tianjin) and MMA (chemically pure (CP), Sinopharm Chemical Reagent Co., Ltd.) at varied mass ratios, along with 2.0 wt% AIBN (CP, Damao Chemicals, Tianjin) relative to the monomers. 98 mL of solvent of anhydrous ethanol (EtOH, CP, QiuZhu Corp. of Sci. & Techn. Tianjin) was then added into each bottle. After complete dissolution of the monomers and the initiator followed nitrogen purge for 5 minutes, all bottles were sealed off, then located on a rotation device and tumbled around a central axis at 10 rpm. A 150 W short arc xenon lamp with focusing optics was directed from the side toward the center of the bottle cluster at a distance of 30 cm. This type of lamp has a continuous spectrum spanning from deep ultraviolet to infrared, and the light was not filtered. The decomposition of the initiator AIBN would take place at wavelengths of 300-400 nm, where the UV absorption of MMA and TMPTMA in ethanol does not overlap. The whole process and the reaction device are illustrated as Scheme 1. To make sure that the reaction was done at the vicinity of ambient temperature, two fans are employed to keep forced draft around bottle clusters. The temperature of reaction mixture was detected at about 25-30 °C, which has been proven having scarcely any effect on the formation of microspheres.<sup>35</sup> The initially homogeneous reaction mixtures turned milky white within 2 to 4 hours of photo-irradiation, depending on the formulation. Unless

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**Table 1** Photoinitiated precipitation polymerization of TMPTMA-MMA in ethanol with varied TMPTMA levels

Run	Crosslinker (wt%)	TMPTMA (g)	MMA (g)	AIBN (g)	D <sub>n</sub> (μm)	D <sub>w</sub> /D <sub>n</sub>	Microsphere yield (%)	Sol. polym. <sup>a</sup> (%)	Conversion (%)	Microsphere formation <sup>b</sup>
A1	0	0	1.888	0.0378	1.2	1.35	13.6	9.8	23.4	Yes
A2	20	0.3860	1.5442	0.0386	1.2	1.02	49.3	8.9	58.2	Yes
A3	40	0.7898	1.1846	0.0395	1.1	1.07	68.7	7.2	75.9	Yes
A4	60	1.2124	0.8083	0.0404	1.0	1.03	77.3	4.8	82.1	Yes
A5	80	1.6553	0.4138	0.0414	0.9	1.05	82.6	2.2	84.8	Yes
A6	100	2.1200	0	0.0424	—	—	—	—	—	coagula

<sup>a</sup> Sol. Polym. referring to the yield of soluble polymer.<sup>b</sup> Observation at 120<sup>th</sup> hour of polymerization.**Table 2** Photoinitiated precipitation polymerization of TMPTMA-MMA in ethanol with varied AIBN amounts<sup>a</sup>

Run	Initiator (wt%)	AIBN (g)	D <sub>n</sub> (μm)	D <sub>w</sub> /D <sub>n</sub>	Microsphere yield (%)	Sol. polym. <sup>b</sup> (%)	Conversion (%)	Microsphere formation <sup>c</sup>
B1	0	0	—	—	—	0.8	0.8	No
B2	1	0.0207	1.3	1.02	72.3	1.5	73.7	Yes
A5	2	0.0414	0.9	1.03	82.6	2.2	84.8	Yes
B3	3	0.0621	0.9	1.25	90.0	4.1	94.1	Yes
B4	4	0.0828	0.8	1.33	95.2	4.4	99.7	Yes

<sup>a</sup> The polymerization was carried out with 80wt% TMPTMA (1.6553 g) and 20wt% MMA (0.4138 g).<sup>b</sup> Sol. Polym. referring to the yield of soluble polymer.<sup>c</sup> Observation at 120 hour of polymerization.

10 otherwise stated all reactions were run for 120 hours.

### Characterization of polymers from photoinitiated precipitation polymerization

Upon polymerization, sample was taken out from the reaction bottle and a few drops of the sample were placed on a glass plate. After evaporation of the solvents at room temperature, the sample was coated by gold sputtering for 400 seconds at 10 KV voltages prior to examination *via* scanning electron microscopy (SEM, Hitachi S-2500, Japan). Microsphere size (D<sub>n</sub>) and size distribution (D<sub>w</sub>/D<sub>n</sub>) was determined by counting at least 50 microspheres from SEM micrographs.

Size and its distribution were also measured using a dynamic light scattering (DLS) instrument (Nano-ZS, Malvern, UK), which can determine microsphere size from 10 nm to 6 μm and gives a particle size distribution curve. The size given is expressed as number average value of all the detected microspheres, and the value of size distribution is provided as PDI, which is regarded as the polydispersity index of the particle size.

The final product was subjected to centrifugation for 5 minutes at 12,000 rpm (Avanti J301, Beckman, USA) in order to separate the microspheres out of the polymerization medium. The supernatant was dried up in an oven at 100 °C for 24 hours in

order to evaluate the amount of the soluble polymer or oligomer, and the sediment microspheres were also dried up to get the microsphere yield. The sum of soluble polymer yield and microsphere yield was considered as the monomer conversion.

The molecular weight of soluble polymers were detected by gel permeation chromatograph (GPC, Waters 2414, USA) via a series of treatment: separating from the reaction mixture, drying at 120 °C and dissolving in tetrahydrofuran. Polystyrene with gradient molecular weights and narrow molecular weight distribution was used as the prototype and tetrahydrofuran was used as eluting agent. Test conditions were set up as follows: column pressure at 290 psi, test temperature at 40 °C and flow velocity of mobile phase at 1 mL per minute.

### Characterization of composite resin containing poly (TMPTMA-MMA) microspheres

The resin matrix was made up of 2,2-Bis-[4-(methacryloxypropoxy)-phenyl]-propane (Bis-GMA), triethylene glycol dimethacrylate (TEGDMA), camphorquinone (CQ, photoinitiator) and dimethylamino-ethyl-methacrylate (DMAEMA, assistant initiator) with the mass ratio of Bis-GMA to TEGDMA at 7:3 or 5:5, CQ amount at 1wt% relative to the total mass of the resin matrix and DMAEMA amount at 2wt%. The resin matrix was stirred for 1 hour with a high speed mixer at

speed of 1000 rotation per minute, then was subject to ultrasonic for 5 minutes to remove bubbles in it. Poly (TMPTMA-MMA) microspheres of 20wt%, relative to the total weight of composite resin, were then added into resin matrix and the mixtures were also stirred for another 1 hour, followed by repeating ultrasonic for 5 minutes.

Thermogravimetric analyzer (TGA, Mettler Toledo, SDTA-851, Switzerland) was conducted to evaluate the phase state of composite resin containing poly (TMPTMA-MMA) microspheres. Samples were put in a platinum crucible and flow velocity of nitrogen was fixed at a rate of 50 mL per minute. The weighing of samples was done by a thermogravimetric analytical balance under the atmosphere of high purity nitrogen, along with heating up from room temperature to 600 °C at a speed of 10 °C per minute.

In addition, the dilatometer (BPZ-1, Botonyc Corp. of Sci. & Techn. Shanghai) was used to determine the volume change of as-resulted composite resin with deionized water as the medium. The sample bottle was connected with the capillary on it via a ground glass stopper. Volumetric shrinkage were calculated according to the change of liquid surface in the capillary before and after light curing reaction. The composite resin with designed volume (V) was put in the sample bottle and the data of capillary at this time was recorded as  $V_1$ . A light curing LED lamp (Coltolux<sup>R</sup> LED, Whaledent Inc) was employed to illuminate on the sample bottle at four directions for 30 seconds, while keeping the light source distance at 1 millimeter. After the curing reaction kept for 60 minutes, the data of capillary was recorded again as  $V_2$ . Volumetric shrinkage ( $V_S$ ) of composite resin was calculated on the basis of the following formula (1), and each group was tested for 5 times to achieve its average value.

$$V_S = (V_2 - V_1) / V \times 100\% \quad (1)$$

For the sake of understanding mechanical property of so-obtained composite resin, it was subjected to a test of microhardness with a digital microvickers hardness tester (HV-5, Botech Co. Ltd., Guangzhou). The composite resin was filled into a mould of  $\Phi$  6mm $\times$ 3mm, and after compaction, both sides of the samples were illuminated for 60 seconds with light curing lamp at room temperature. The samples after demoulding were exposed at room temperature for 3 days. Hereafter, the surface of both sides was rubbed down with an abrasive paper of silicon carbide. The samples were finally put in the hardness tester for 10 seconds at a loading of 1.96 N, to achieve the hardness value. Each group was tested with 5 samples.

## Results and discussion

It was widely reported that monomers used in precipitation polymerization were well dissolved in solvents, but oligomers formed in initial stage would sedimentate out from the solvents once the molecular chain of oligomers reached a critical chain length, entangled and aggregated to form primary particles. The as-resulted primary particles would continue to grow up until the exhaustion of initiators or monomers.<sup>37-41</sup> The entropy mechanism proposed by Stöver *et al*<sup>37</sup> suggested that the growth of primary particles depended largely on the presence of soluble terminal segments of polymers on microsphere surface. These segments endowed the primary particles with good stability since they were rich in residual double bonds of crosslinkers and were the key

source to enlarge the primary particle with monomers or active oligomers.

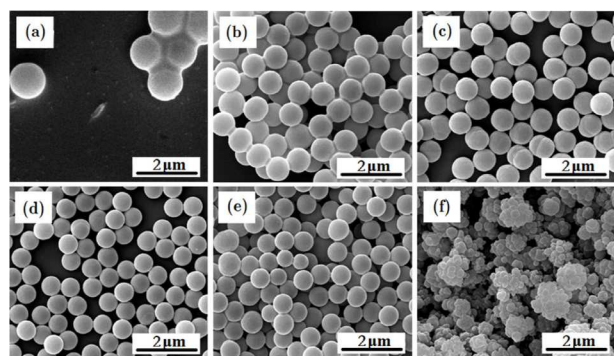
Based on extensive research work on thermal inducing precipitation polymerization, a variety of parameters, including crosslinker amounts, monomer concentrations, solvent type and initiator contents, were well-established. Those parameters, however, were necessary to be reestablished in present protocol, because the reaction was needed to take place in a completely redesigned environment. Our previous work proved that monodisperse microspheres could be achieved free of coagula by copolymerization of TMPTMA and Styrene in the mixed solvents of ethanol and water, but particle aggregates were found by *homo*-polymerization of TMPTMA.<sup>42</sup> Therefore, the adoption of TMPTMA as crosslinker in photoinitiated precipitation polymerization of methacrylate monomers may open up a new avenue to fabricate microspheres.

### Effect of Crosslinker

In order to establish an appropriate protocol, photoinitiated precipitation polymerization of TMPTMA and MMA, at monomer concentration of 2 vol%, were carried out in the solvent of ethanol with different TMPTMA/MMA ratios. The results were given in Table 1, and selected SEM micrographs were shown in Figure 1. The particle size ( $D_n$ ) and size distribution ( $D_w/D_n$ ) were obtained from SEM photos of the samples by counting about 50 microspheres. Table 1 indicated that microspheres were readily formed without TMPTMA or with TMPTMA levels equal to or less than 80 wt% in the monomer mixture, although the coagula were concomitantly observed when TMPTMA higher than 80 wt%. In the run free of TMPTMA, no perceptible polymerization was detected during the first 24 hours. However, the reaction was found when it was extended to 48<sup>th</sup> hours. The reaction was kept to 120 hours with a monomer conversion of 23.38% detected.

Table 1 showed that the final monomer conversion increased regularly along with the increase of TMPTMA. This indicated that the polymerization was closely related to or controlled by particle formation, which was in agreement with entropic capture mechanism of oligomers in this polymerization,<sup>37</sup> and implied that soluble polymers or oligomers were captured from the solution by vinyl groups on the particle surface throughout the whole polymerization.<sup>41</sup> High monomer conversion would not be achieved without the formation of a large amount of particles, as is the case at a low level of TMPTMA.

From Table 1, a broader size distribution was observed for the run of *homo*-polymerization of MMA. The broader size distribution was probably a result of a delayed and extended particle nucleation because oligomers of pure MMA were not crosslinked. When the polymerization was extended to 48<sup>th</sup> hour, new particles were still being formed and particle nucleation was not fully accomplished and a huge number of primary particles were present. The growing particles would coalesce and lead to a broader size distribution. The data in Table 1 also revealed that the particle size decreased in a regular manner with an increase in TMPTMA level, owing to the fact that, with the presence of more TMPTMA, particle formation after sedimentation of oligomers was accelerated due to the reduced solubility as a result of higher crosslinking and, therefore, more particles were formed, which



**Fig. 1** SEM of Microspheres prepared *via* photoinitiated precipitation polymerization of TMPTMA-MMA with varied TMPTMA levels: (a) 0%, (b) 20%, (c) 40%, (d) 60%, (e) 80%, (f) 100%.

would lead to smaller particle sizes. The microsphere yields in Table 1 were quite high when compared to those in previous reports on the photoinitiated precipitation copolymerization of difunctional crosslinkers and methacrylate monomers, which was no more than 13.2%.<sup>36</sup> This suggested that, the change of crosslinkers from difunction to trifunction and therefore the increase of crosslinking groups, resulted in the improvement of microsphere yields. So the use of trifunctional crosslinker of TMPTMA was demonstrated an effective approach to improve microsphere yields based on methacrylate monomers.

The SEM photos in Figure 1 intuitively revealed the morphology of resulted microspheres. As TMPTMA amounts ranged from 20% to 80%, the microspheres with narrow size distributions and smooth surface were achieved, although their sizes became smaller, as is indicated in Table 1, that varied from 1.15  $\mu\text{m}$  to 0.94  $\mu\text{m}$ . Outside this range, irregular polymer productions were found, *e.g.* the homo-polymerization of MMA led to seriously adhesive microspheres with broader size distribution and the use of only TMPTMA resulted in lots of coagula, obviously which were formed from the coalescence of huge number of primary particles. It follows that, in order to obtain monodisperse microspheres, moderate amount of TMPTMA was necessary in polymerization ingredient.

### 30 Photoinitiation conditions

In light of the fact that all the chemicals in the reaction bottle, *e.g.* crosslinker, MMA, and AIBN, except solvent are photoexcited, this remains the possibility of independent photoreactions of photoexcited crosslinker and/or MMA. To verify the possibility, we have carried out the reaction without the use of AIBN, with other reaction conditions kept as follows: mass ratio of TMPTMA /MMA at 80/20, monomer concentration at 2wt%. No polymer particles were observed by SEM even after 120 hours of photoirradiation, the conversion rate of monomers approached only 0.8%. The results demonstrated that independent photoreactions of photoexcited crosslinker and/or MMA indeed existed, but the as-prepared polymer is insufficient to form primary particles.

In order to have an optimized photoinitiation condition, we further carried out the polymerization with different amounts of AIBN, *e. g.* 0, 1%, 2%, 3% and 4% by weight, and other

conditions remained unchanged (mass ratio of TMPTMA /MMA at 1:1, monomer concentration at 2%). At designed reaction time, the monomer conversions were detected. The curves resulted from conversion vs reaction time were shown in Figure 2.

It was clearly seen from Figure 2 (a), all of the polymerizations with different AIBN amounts had an obvious induction period, and the induction period was shortened with addition of AIBN. The conversion of MMA and TMPTMA was slightly increased after about 24 hours when AIBN was not included. With the addition of 1% of AIBN, the reaction took up at the second hours. When the amounts of AIBN increased to 3%, the induction period was even shortened to nearly 1 hours. With 4% of AIBN, half an hour was enough to trigger the polymerization. It was easy to understand, that certain amounts of AIBN consumed in the induction period, and increasing AIBN was helpful for improving efficiency of photoinitiated precipitation polymerization.

SEM micrographs displayed in Figure 2 (b-e) showed microspheres in the four samples prepared with AIBN concentrations that ranged from 1% to 4%. It can be found, the sizes got smaller on the whole and the size distribution became broader, as the photoinitiator increased in the polymerization. At 1% of AIBN, uniform microspheres with uneven surface were achieved. When AIBN amount was added up to 2%, the surface of microspheres became much smoother. However, further increase of AIBN, resulted in an expected phenomenon that much wider size distribution and serious adhesion of numerous primary particles on microsphere surface appeared.

With the purpose to fully reveal the impact of initiator on the polymerization, the reaction systems, including parallel polymerizations with varied AIBN concentration while keeping monomer concentration at 2% and TMPTMA/MMA ratio at 80/20 by weight, was further analyzed, and the results were collected in Table 2. For the runs with 1% AIBN and above, they readily proceed within 120 hours. It is found that the greater the initiator amount, the higher the final conversion. At 4% of AIBN, the monomer conversion reached a highest value of 99.68% among all the runs. More initiator would have led to a shortened nucleation period, and as a consequence, more primary particles formed. In this case particle size would finally decrease since monomer concentration was kept at a same level for all the runs. It was worth noting that a monomer conversion of nearly 85% or higher was easily achieved with AIBN at 2% or higher. In Table 2 was also presented the quantity of soluble polymer or oligomer. In general, the proportion of soluble polymer increased along with the increase of AIBN, which was likely an indication that more oligomers were also formed during the polymerization.

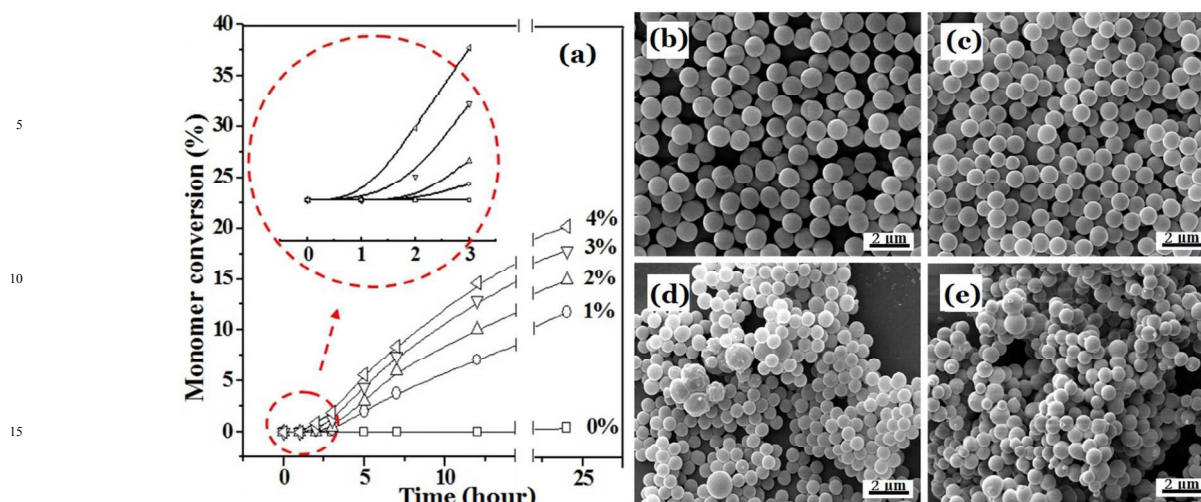
### Tracking analyses on photoinitiation precipitation polymerization

To make a thorough inquiry on the formation of methacrylate based polymer microspheres, the evolutions of monomer conversion, microsphere yield and soluble polymer yield in polymerization of Run A5 were all tracking analyzed at first. Results were plotted in Figure 3, which revealed that the polymerization evolved at a rapid speed after a two-hour induction period, and followed by a slow-down until 100<sup>th</sup> hours, where monomer conversion reached nearly its final value. The

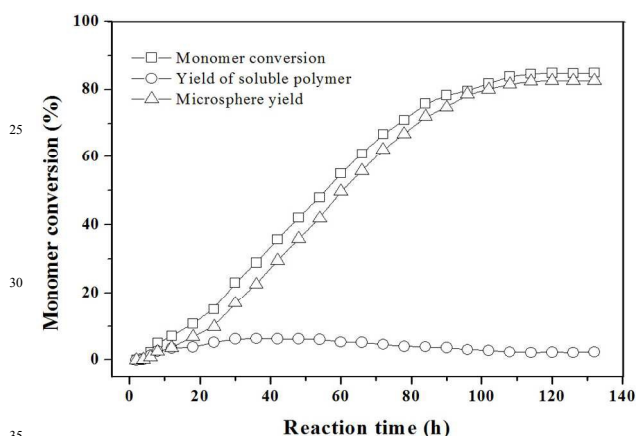
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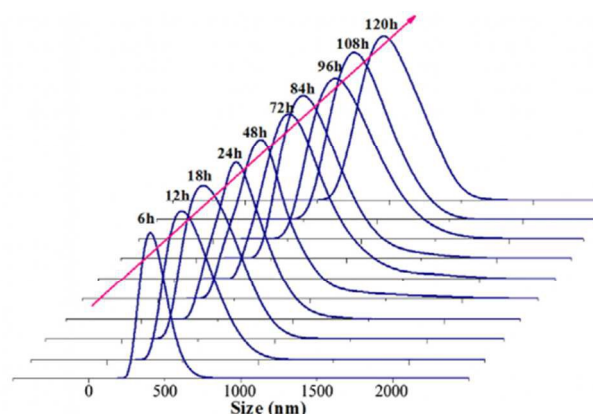
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**Fig. 2** Variation of Monomer conversion (a) and SEM of resulted microspheres in photoinitiated precipitated polymerization of TMPTMA-MMA with different AIBN amounts: 1% (b), 2% (c), 3% (d) and 4% (e).



**Fig. 3** Evolution of monomer conversion, microsphere yield and soluble polymer yield in photoinitiated precipitation polymerization of TMPTMA-MMA in ethanol.

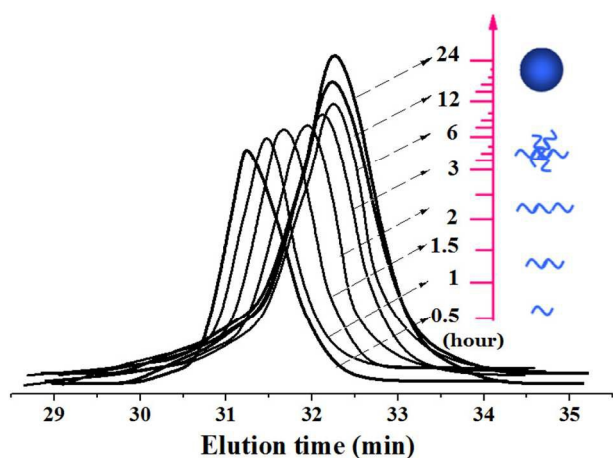


**Fig. 4** Size and size distribution of microspheres prepared by photoinitiated precipitation polymerization of TMPTMA-MMA at different polymerization time.

evolution of microsphere yield was in good agreement with the monomer conversions, though it was always less than the latter, due to the fact that monomer conversion was just the summation of microsphere yield and soluble polymer yield. Soluble polymer yield remained a slow decrease for 60 hours after a slight increase in the first 40 hours, then followed by an unobvious variation. The monomer conversion had no perceived change after 120 hours, which was regarded as a sign of reaction ceasing. The formation mechanism of microsphere in photoinitiated precipitation polymerization, based on the above observations, was further deduced as follows: The oligomers formed in the earlier stage, followed by an increase of not only the amount but also the molecular weight. When the oligomers increased to a critical chain length, which has been mentioned for many times in

the relative reports,<sup>37-39</sup> they aggregated into primary particles, then continue to grow up to form microspheres. Many groups demonstrated one fact that exposed double bonds of crosslinkers on microsphere surface could continuously capture the soluble polymer, which played an important role in the enlargement of microspheres.<sup>37-41</sup> Accordingly, the concentration of soluble polymers or oligomers would decrease in the wake of microsphere growth. But the consumed amounts of soluble polymer or oligomer were constantly replenished through further polymerization of remained monomers triggered by residual initiators, that's why soluble polymers or oligomers would still stay at a relatively stable level in the end, rather than being used up.

In addition, size and size distribution of microspheres at



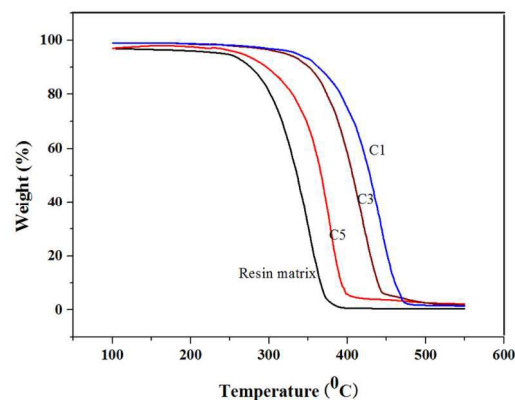
**Fig. 5** GPC traces of soluble polymer obtained in photoinitiated precipitation polymerization of TMPTMA-MMA at different polymerization time.

different time were analyzed by DLS with the results shown in Figure 4. It was found that little particles with size of 300 nm formed at 6<sup>th</sup> hour. Those particles have kept continuously growing until 100<sup>th</sup> hour, whereafter no enlargement of microspheres was found. The size distribution had a corresponding variation to the size. The primary particles possessed narrow size distribution at initial stage, which gradually turned much wider until 100<sup>th</sup> hour, whereafter, the size distribution became narrow again. Based on above facts, the reason for the variation of size and its distribution was tentatively revealed. As mentioned previously, the solubility of oligomers in the solvent decreased to form nucleus at initial stage, thus large number of primary particles at nanoscale were achieved. The change of size distribution which became wider from 6<sup>th</sup> to 100<sup>th</sup> hour was resulted from the coalescence of primary particles.<sup>37</sup> Owing to the fact that double bonds on microsphere surface could capture soluble polymers or oligomers, the microspheres were continuously growing. As is known that the smaller the particle, the larger the surface area, small particles were easy to capture more soluble polymers or oligomers to enlarge themselves than larger ones, thus on the whole, size distribution of microspheres tended to be narrow again at the final stage.<sup>38</sup>

Finally, the evolution of soluble polymer in the polymerization was also followed by GPC with the results shown in Figure 5, which indicated both molecular weight and oligomer contents gradually increased in the first 6 hours. Molecular weight kept unchanged at about 2070 grams per mole from then on, however the content of oligomers increased gradually. Obviously, the variation of oligomers coincided with the results from Figure 3 and Figure 4, which further provide an evidence for the existence of critical chain length of soluble polymers. When soluble polymers increased to critical chain length, they became indissolvable with the solvent and sedimentated to form primary particles.

#### 40 Performance of composite resin containing poly (TMPTMA-MMA) microspheres

As mentioned above, the as-resulted poly (TMPTMA-MMA) microspheres were prepared to serve as organic fillers in dental



**Fig. 6** TGA curves of composite resins containing poly (TMPTMA-MMA) microspheres as organic filler and resin matrix of Bis-GMA and TEGDMA.

restorative materials, so the compatibility between organic fillers and resin matrix and the inner phase behavior of composite resin should be firstly explored. It is known that thermogravimetric analysis (TGA) technique could give lots of informations about chemical composition and structure of composite materials, thus the so-obtained composite resins containing organic filler of poly (TMPTMA-MMA) microspheres were analyzed by TGA, with the results shown in Figure 6. Thermogravimetric curves of all the samples had a similar shape, namely a one-off degradation curve, in spite of the fact that they took place at different temperatures. This suggested that a homogeneous phase state existed in these composite resins, which was easy to combine with the fact that similar molecular structures of MMA and TMPTMA resulted in good compatibility between them as well as the resin matrix containing also methacrylate type monomers. The thermal degradation temperature can indirectly reflect the mechanical properties of composite resins, which were the important parameters for the potential application as dental restorative materials. The temperatures corresponding to 50% of weight loss rate (WLR) was used as a standard to this end. Figure 6 showed that, when TMPTMA increased from 20 to 80wt%, the temperatures with regard to 50% WLR of Samples C5 to C1 increased from 366 °C to 429 °C, while that of the resin matrix was only 334°C. The results indicated the performance of composite resins could be significantly improved by adjusting crosslinker dosages in the micrpspheres.

Hardness of composite resin can also reflect its mechanical performance<sup>43,44</sup> Table 3 showed the microhardness of composite resins containing poly (TMPTMA-MMA) microsphere at different amounts. The microhardness increased with the increase of crosslinker amounts. This is because that network structure in poly (TMPTMA-MMA) microsphere became more intensive and more likely to hinder rotation or movement of molecular chains along with increasing degree of crosslinking.<sup>45</sup> Accordingly, it resulted in enhanced rigidity and increasing hardness of composite resins.

It is worth noting that the hardness of composite resin is also affected by filler amounts. The amounta of organic filler added in the composite resin were all around 20wt%, thus the hardness of



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**Table 3** Composite resins with poly (TMPTMA-MMA) microspheres as organic filler at different amounts

Run	Organic fillers <sup>a</sup>			Resin matrix <sup>b</sup>			Microhardness (HV)	Volumetric shrinkage (%)
	Crosslinker (wt%)	TMPTMA (g)	MMA (g)	Bis-GMA (wt%)	Bis-GMA (g)	TEGDMA (g)		
C1	80	1.6553	0.4138	70	0.1542	0.0661	22.2	3.3
C2	80	1.6553	0.4138	50	0.1102	0.1102	21.5	3.6
C3	60	1.2124	0.8083	70	0.1542	0.0661	20.7	3.6
C4	60	1.2124	0.8083	50	0.1102	0.1102	20.5	3.7
C5	20	0.3860	1.5442	70	0.1542	0.0661	19.8	3.8
C6	20	0.3860	1.5442	50	0.1102	0.1102	19.7	4.0
C7	Samples (Filtek Z250) from 3M company						45.2	4.3

<sup>a</sup> The amount of poly (TMPTMA-MMA) microspheres was fixed at 20wt% relative to the total weight of composite resin. The weights of TMPTMA and MMA were referred to that used in photoinitiated precipitation polymerization.

<sup>b</sup> The amount of resin matrix was fixed at 80wt% relative to the total weight of composite resin. The weights of Bis-GMA and TEGDMA were referred to that used in composite resin samples for microhardness test.

those materials had no obvious difference. However, the hardness of the composite resin (Filtek Z250) provided by 3M company was detected with the value up to 45.2 HV. The reason why hardness of our products was much lower than that from 3M company is considered as follows: The fillers added in the composite resin of 3M company were of inorganic compounds, including zirconia and anhydrous silicate, which have greater hardness than organic materials. Meanwhile, the filler amount of composite resin from 3M company, equal to 60wt%, is higher than that with poly (TMPTMA-MMA) microspheres.

When Bis-GMA in resin matrix was partially replaced by TEGDMA, the hardness of composite resin was found markedly reduced. Composite resin C1 with 80wt% of TMPTMA and 70wt% of Bis-GMA had the highest hardness, up to 22.2 HV. Musanje's group<sup>46</sup> and Asmussen's group<sup>47</sup> have also reported the similar observation and thought it was resulted from the formation of rigid polymer network through hydroxy group of Bis-GMA. Compared with TEGDMA, Bis-GMA was easy to form more compact network structure, thus led to higher hardness.

Volumetric shrinkage is also a major parameter for dental restorative materials. It could be seen from Table 3, with the increase of TMPTMA, volumetric shrinkage of composite resins was gradually lowered down. Among all the samples, Run C1 had the lowest volumetric shrinkage. Obviously, the increase of crosslinker led to significant resistance to volume change. In addition, volumetric shrinkage increased along with the diminishing ratio of Bis-GMA to TEGDMA. This indicated that volumetric shrinkage of composite resin was also in the control of relative amount of Bis-GMA and TEGDMA. Finally, volumetric shrinkages of so-obtained composite resin were close to or lower

than that of 3M company. In a word, good compatibility between polymer microspheres based on MMA monomers and resin matrix containing Bis-GMA and TEGDMA, coupled with high hardness stemmed from crosslinked microspheres, contributed largely to the low volumetric shrinkage.

## Conclusions

Pure and crosslinked polymer microspheres with undoped methacrylate monomers were prepared *via* a green approach, in which photoinitiated precipitation polymerization of MMA and TMPTMA, was carried out in a low-toxicity solvent at room temperature. The way to improve microsphere yield was explored, with the results that the microsphere yield could be significantly improved by increase of trifunctional crosslinker as well as the photoinitiator. Especially, microsphere yield was even up to 95.24 at 80% of TMPTMA and 4% of AIBN, which was significantly higher than that done with EGDMA or DVB. To make a thorough inquiry on how methacrylate based polymer microspheres formed, the evolution of photoinitiated precipitation polymerization was tracked and the formation mechanism of poly (TMPTMA-MMA) microspheres was also elucidated. The existence of critical chain length was verified for the first time with the results from GPC. Because of good compatibility between polymer microspheres based on MMA monomers and resin matrix containing Bis-GMA and TEGDMA, coupled with high hardness from crosslinked microspheres, the so-obtained pure microspheres were proved to have large possibility to serve as organic fillers in dental restorative materials.

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## Notes

<sup>a</sup> Shandong provincial engineering laboratory of novel pharmaceutical excipients, sustained and controlled release preparatoin, College of medicine and nursing, Dezhou University, Dezhou, China. Fax: 86-534-898-9506; Tel: 86-534-898-9506; E-mail: hanwen916@163.com

<sup>b</sup> College of Chemistry and Chemical Engineering, University of Jinan, Jinan, China. Fax: 86-531-8276-7725; Tel: 86-531-8276-7725; E-mail: xzkong12@yahoo.ca