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ORIGINAL CONTRIBUTION

Lee G. Stanek
Steven M. Heilmann
William B. Gleason

Preparation of monodisperse PMMA microspheres using 2-vinyl-4,4′-dimethylazlactone as a particle Stabilizer

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L. G. Stanek · W. B. Gleason (✉)
Department of Chemistry,
University of Minnesota,
Minneapolis, MN 55455, USA
E-mail: bgleason@umn.edu

S. M. Heilmann
Organic Materials Technology Center,
3M Company, St. Paul, MN 55144, USA

W. B. Gleason
Department of Laboratory
Medicine & Pathology,
University of Minnesota,
Minneapolis, MN 55455, USA

Abstracts Polymeric microspheres of methyl methacrylate (PMMA) have been prepared via emulsion polymerization using potassium persulfate as initiator. The polymeric spheres were also prepared with varied concentration of an additional component, 2-vinyl-4,4′-dimethylazlactone (VDMA), which greatly affected the properties of the spheres. NMR analysis indicates the presence of VDMA in the polymer particles, and FT-IR analysis shows hydrolysis of VDMA in the polymer which produced *N*-acryloylmethylalanine, (NAMA). The VDMA hydrolysis thus led to carboxyl functionality which served to stabilize the microspheres during the emulsion polymerization showing a significant effect on particle size, distribution, and morphology, but little effect on molecular weight or thermal properties of the polymer. Also the effect of varying the concentration of initiator (potassium persulfate, KPS) was investigated, and had little effect on particle size or distribution or molecular weight of the polymer particles.

Keywords Emulsion polymerization · PMMA · Azlactone · Polymerizable surfactant · Amino acid

Introduction

Polymeric latex particles are utilized in a wide range of applications, with numerous examples in recent years of biomaterial and biotechnological applications. In particular, drug delivery systems comprised of polymeric particles have become a significant area of research. Controlled release of a therapeutic agent is a desirable characteristic for a drug delivery system, allowing for a consistent dosing rate compared to more traditional drug administration methods [1]. Recently, advances in the use of polymeric materials in controlled release technologies have included biodegradable polymers such as polylactide, polyglycolide, or lactide/glycolide copolymers [2–4]. However, biodegradation of the polymeric matrix may result in detrimental effects in the physical properties of the bulk material when used in load bearing applications where drug delivery is also a requirement.

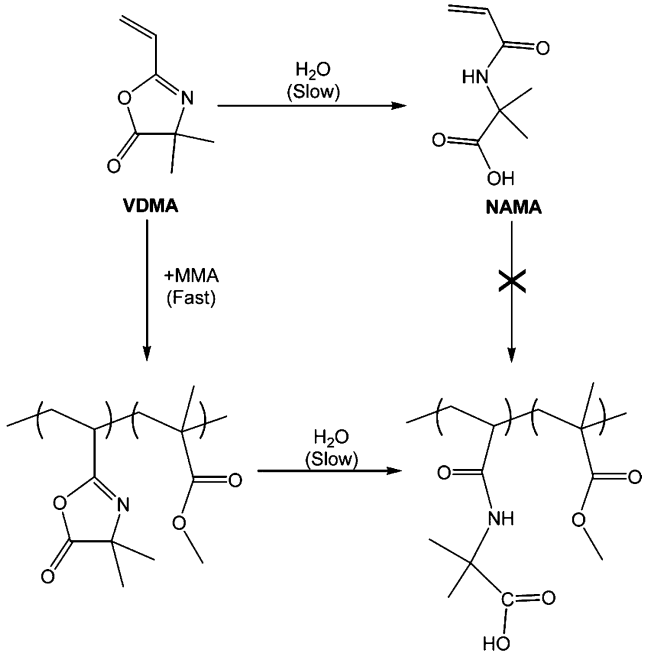
Poly(methyl methacrylate) (PMMA) is an excellent example of a structurally robust polymeric material suitable for use as a therapeutic carrier in a variety of applications [1, 5]. Previously, PMMA polymeric materials have found use in biomaterial applications that take advantage of its rigid polymeric structure, optical clarity, or non-biodegradability. These applications include uses in ophthalmologic restorations, intraocular lenses, and particularly as a major component of bone cement [1, 5, 6]. Previously, it had been shown that PMMA latex particles can be used in a variety of other drug delivery applications, as well. For example, Lee et al. [7] describe the increased stabilization of vitamin A by encapsulation in poly(ethyleneimine) grafted microspheres of PMMA. In addition, advances in bone cements used in bone-prosthetic joining applications have been made, specifically in drug containing materials. Specifically, antibiotics (e.g. gentamicin) have been incorporated into

the solid portion of the cement composition and mechanically mixed with the other ingredients when the powder and liquid phases are combined [5]. There are numerous examples showing prolonged release of antibiotics from such bone cements, however the amount of released therapeutic is greatly reduced over time, increasing the possibility for long-term complications due to infection [5]. Thus, in this application, efforts are being directed toward synthesis of polymeric materials for potential covalent attachment of antibiotics that would help maintain higher levels of antibiotic activity over longer periods of time.

Covalent binding of biologically active molecules to a polymeric substrate has advantages over encapsulation technologies where problems associated with unwanted leaching or bulk dumping of the biomolecule may have detrimental impact [8]. Recent work by Sivakumar and Rao [9] demonstrated that functional PMMA microspheres may be prepared and utilized for in vitro release of ibuprofen and gentamicin for extended periods of time compared to non-functionalized PMMA. Also, Tao et al. [10, 11] have demonstrated attachment of lectins using avidin–biotin coupling to amine functionalized PMMA.

Overall, the ability to have both encapsulated antibiotics and immobilized antibiotics in a biomaterial could greatly decrease the number and frequency of implant complications. Therefore, in combination with encapsulation, covalent immobilization of antibiotics to polymeric substrates for application in drug delivery technology would advance the methodology already in place, especially for bone cements, orthopedic restorations or ophthalmologic implants.

In this paper, we describe the synthesis and characterization of PMMA microparticles using varied emulsion polymerization conditions. The addition of 2-vinyl-4,4′-dimethylazlactone (VDMA) resulted in copolymerization with methyl methacrylate (MMA) followed by efficient hydrolysis of the azlactone ring, which results in carboxyl functionality in the polymer particles and allowed for particle stabilization. Emulsion polymerizations were monitored as a function of weight percent VDMA and initiator concentration (potassium persulfate, KPS). Analysis of the polymer particles indicates the ability to maintain spherical particle morphology with consistent particle size and polymer molecular weight when 32 Wt. % percent VDMA was used under varied concentration of KPS. It was also apparent that the addition of VDMA to the emulsion reaction resulted in copolymerization with MMA followed by hydrolysis, thus playing a vital role in maintaining narrow particle size distribution.



Sch. 1 Routes of water hydrolysis of 2-vinyl-4,4′-dimethylazlactone (VDMA) to produce *N*-acryloylmethylalanine (NAMA) or to copolymerization followed by hydrolysis

Experimental

Materials

Methyl methacrylate (MMA) was purchased from Aldrich Chemical Company (Milwaukee, WI, USA). MMA was passed through a glass column containing Inhibitor Remover (Aldrich Chemical Company) to remove hydroquinone monomethyl ether (MEHQ) and stored at 4°C. 2-Vinyl-4,4′-dimethylazlactone (VDMA) was obtained from SPNE (Princeton, NJ, USA). VDMA was vacuum distilled at 60°C and a pressure of 5.0 in. of Hg (with a regulated air bleed), in the presence of 0.2% (w/v) butylated hydroxytoluen (BHT) and 1.0% (w/v) anhydrous sodium carbonate, and stored at 4°C. All other reagents were obtained from Aldrich Chemical Company (Milwaukee, WI, USA), and used as received. Solvents were of reagent grade or higher and used as received.

Emulsion polymerization of MMA

The following describes a representative emulsion polymerization procedure. A 500-mL, 3-neck round-bottom flask was equipped with a mechanical stirring apparatus, cold water condenser, argon inlet, and temperature monitoring thermocouple. To the flask was added 190.0 mL of HPLC-grade water, 39.0 mL of MMA and

11.0 mL of VDMA (4:1 v/v ratio, water:monomer). The reaction mixture was sparged for 15 min with argon and heated to 55°C, when solid began to precipitate. (VDMA hydrolysis kinetics indicate the solid is NAMA, data not shown). Potassium persulfate (KPS, $K_2S_2O_8$) (0.250 g in 10.0 mL water, 200.0 mL total volume water) was added to initiate the polymerization. Heating continued for 10 minutes until the temperature reached 70°C. After 1 h of reaction, the temperature increased sharply to greater than 80°C, and then cooled back to 70°C, while a large amount of white solid precipitated. After 2 h of total reaction, the mixture was allowed to cool for approximately 15 min to below 40°C. The white floculant mass was removed from the reaction flask with large amounts HPLC-grade water, vacuum filtered, and collected. Polymer was then resuspended in stirring methanol for 24 h, vacuum filtered and freeze-dried.

Scanning electron microscopy (SEM)

Scanning electron microscopy (SEM) was conducted using a JEOL JSM 6500 Field-Emission Gun Scanning Electron Microscope (FEGSEM). The samples were coated with 50 Å of platinum, with working distances between 5.4 and 8.5 mm.

Light scattering analysis

Light scattering experiments were conducted on a Coulter LS-230 Small Volume module with methanol or water as the suspending solvent for the PMMA particles.

NMR analysis

^{1}H-NMR was conducted on a Varian Inova 300 MHz spectrometer using *N,N*-dimethylformamide (DMF- d_7) as solvent. Spectra were taken at 80°C for improved spectral resolution.

SEC analysis

Size-exclusion chromatography (SEC) analysis was conducted on a HP SEC system with a HP 1074A refractive index detector, an Agilent 35900E analog to digital signal converter with Agilent Technologies software for molecular weight determinations. The system was equipped with a Jordi DVB (divinylbenzene) three-column set with column pore sizes of 10^4, 10^3, and 500 Å. The system was calibrated with polystyrene standards of molecular weights ranging from 10^3 to 4×10^5 g/mol. All samples were dissolved in degassed, HPLC grade tetrahydrofuran (THF) at concentrations of 10 mg/mL, and filtered using 0.2-μm PTFE filters. The samples were analyzed at a flow rate of 1.0 mL/min, an injection volume of 50 μL, and a column temperature of 40°C.

FTIR spectrometry

Fourier-Transform Infrared spectrometry was conducted on a MIDAC M2000 Series FTIR equipped with single beam detector and GRAMS/AI software from Thermo Electron Corporation. Samples were prepared as 10% nujol mull and analyzed using sodium chloride salt plates and 32 scans.

DSC analysis

Differential scanning calorimetry (DSC) was performed on a Perkin-Elmer DSC-7 instrument with copolymer samples of 5–10 mg weighed in aluminum DSC pans. The polymers were subjected to the following heating cycle: (1) Heat from 50 to 250°C at 20°C; (2) Hold at 250°C for 1 min; (3) Cool from 250 to 50°C at 50°C min;

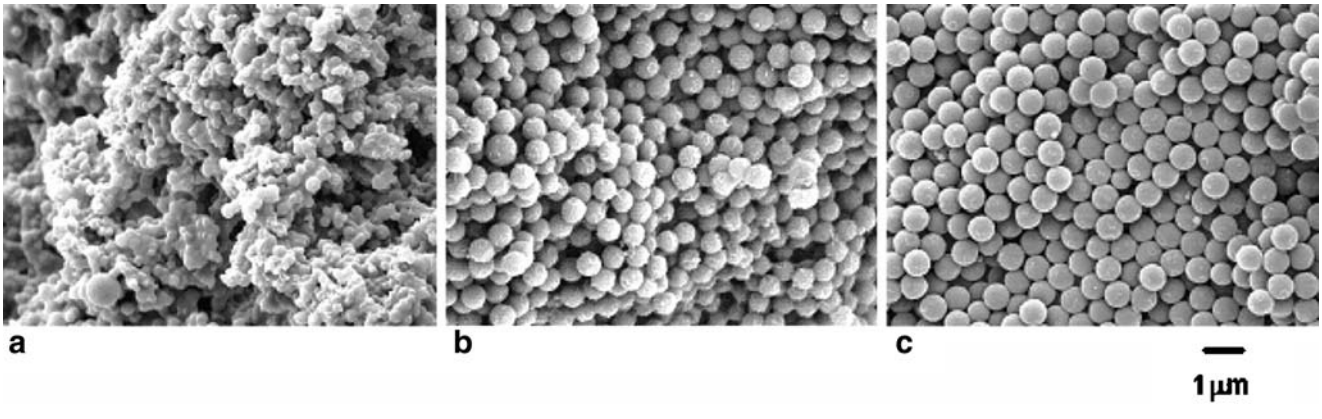


Fig. 1 Representative SEM micrographs of PMMA particles prepared with varying weight percent of VDMA **a** 12 Wt. %, **b** 23 Wt. %, and **c** 32 Wt. %, while holding the concentration of KPS constant at 0.0055 M

(4) Hold for 1 min at 50°C; (5) Heat from 50 to 250°C at 10°C min. Glass transition temperatures (T_g's) were calculated by extrapolating the two linear regions of the plot before and after the change in heat capacity.

Results and discussion

Varying concentration of VDMA

Polymeric microspheres described in this section were prepared using a constant initiator concentration of 0.0055 M KPS with varying weight fraction of VDMA to MMA. The weight percent of VDMA was varied in order to determine the effect on particle size and particle size distribution, polymer molecular weight, and thermal characteristics.

Scanning electron microscopy allowed for the imaging of sub-micrometer sized PMMA particles in order to gain an understanding of particle morphology, and allowed for visual inspection of the particles prepared under these emulsion polymerization conditions. SEM images of the particles are shown in Fig. 1, and they indicate that as the weight fraction of VDMA decreased, the amount of coagulation of the particles increased. This was probably a result of destabilization of the particles because of a lower weight percent of VDMA, which corresponds directly to a smaller fraction of carboxyl functionality in the particles. In this work, particle stabilization is afforded by VDMA first undergoing copolymerization with MMA, followed by hydrolysis of the azlactone ring to give an *N*-acryloylmethylalanine (NAMA) containing polymer particle of poly(NAMA-*co*-MMA). The carboxyl groups of NAMA are able to participate in hydrophilic interactions with the aqueous phase and stabilize the polymer particles. Also, the carboxyl groups at the surface of the particles decreased the likelihood of coagulation by inducing charge repulsion at the surface of the particle.

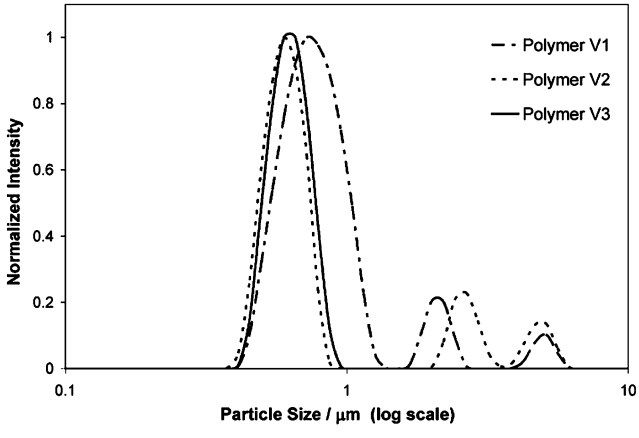


Fig. 2 Particle size data for PMMA spheres prepared with varying weight fraction of VDMA added versus MMA

These effects are similar to those seen in emulsion polymerizations with polymerizable surfactants [12–14]. Polymerizable surfactants allow for increased stabilization of polymeric particles, and maintain morphology through polymerization into the particle [13]. Thus allowing for decreased surfactant migration during processes such as film casting or flocculation where maintaining particle size and dimension is of critical importance [13].

Particle size analysis by light scattering (Fig. 2) showed that polymer particles with lower amounts VDMA had overall higher particles diameters, and showed two side peaks in the distribution curve toward higher particle diameters. These side peaks result in an increase in the coefficient of variance for the particles, which are often used as an index of dispersity for colloidal particles. Low CV values indicate a highly monodisperse latex, and higher CV values indicate an increase in the degree of polydispersity of particle size. Typically, CV values for highly monodisperse particles, such as those used as instrument calibration standards, range from 1 to 5%. The results shown here indicate CV values for lower weight percent VDMA to be much larger (84–107%) than those prepared with 32 Wt. % VDMA (16%). At 32 Wt. % VDMA, the side peaks are absent and the particle size data indicate more monodisperse particles. Additionally, for polymer V0, when no VDMA is added to the emulsion preparation, the particle diameters increases drastically to about 38 µm with a much broader distribution in particle size (CV = 58%). This data, when compared to previous experiments, shows still higher particle sizes compared to PMMA microspheres initiated by KPS at a much higher concentration [15].

After examining the data given in Figs. 1 and 2 and Table 1, it was determined that copolymerization of VDMA and MMA prior to hydrolysis was the significant step in creating the monodisperse particles. Therefore, it was important to investigate whether NAMA itself was capable of undergoing copolymerization with MMA under the same emulsion conditions, to rule out the possibility of copolymerization after VDMA hydrolysis. As can be seen in Fig. 3, the particles

Table 1 Particle size statistics obtained from light scattering of polymeric dispersions in methanol

Polymer[a]	VDMA Wt %[b]	Mean particle diameter (µm)	Standard deviation (µm)	Coefficient of variance (%)
V0	0	38.7	22.7	58.5
V1	13	1.058	0.882	83.4
V2	23	1.230	1.312	107
V3	32	0.661	0.104	15.7

[a]All polymers prepared using [KPS] = 0.0055 M
[b]Weight percent of VDMA added versus weight of MMA

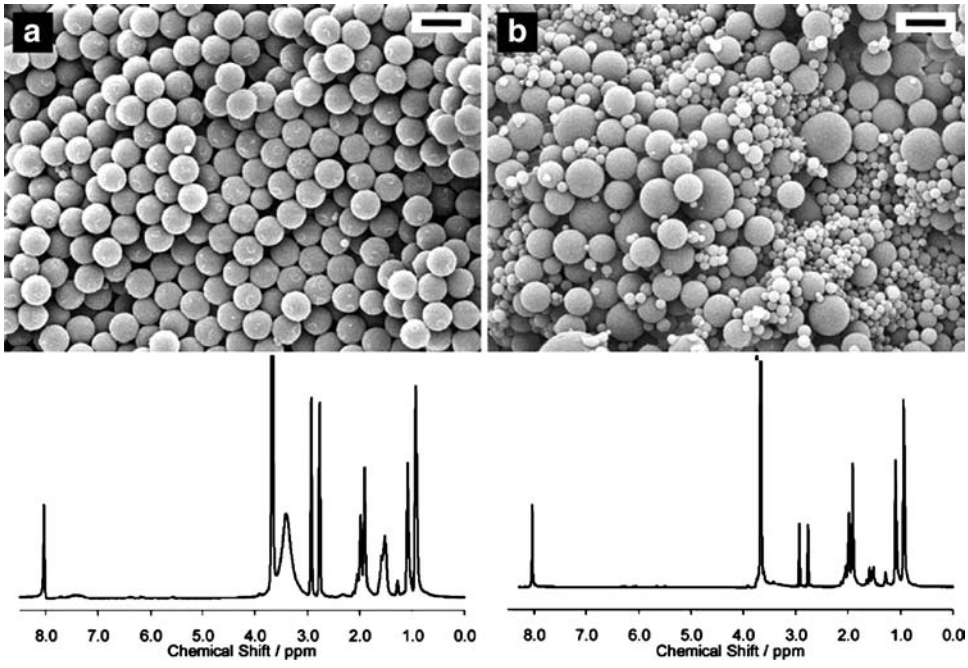


Fig. 3 Representative SEM micrographs comparing particles prepared with VDMA (**a**) versus NAMA (**b**) including their corresponding ^{1}H-NMR spectra below

prepared with 32 Wt. % of VDMA showed uniform particle size (Polymer V3). When an analogous experiment was conducted using 32 Wt. % of NAMA, the resulting particles were no longer monodisperse. Light scattering analysis confirmed the larger size and broader particle size distribution with NAMA, with a CV of 76.4%, which was much higher than the 16% for polymer V3. Particles prepared with added VDMA show specific peaks in the ^{1}H-NMR spectra that indicate the presence of hydrolyzed VDMA in the copolymer via resonances at 7.4 and 1.5 ppm. These peaks are not present in the NMR spectra of the particles prepared with NAMA, indicating NAMA and MMA do not copolymerize (See Fig. 3). This experiment solidified the hypothesis that VDMA is incorporated into PMMA particles through copolymerization, and the subsequent hydrolysis of the azlactone ring results in carboxylic functionality that enhances particle stabilization. The extent of incorporation, as determined by integration of proton-NMR indicated that VDMA was incorporated into the particles between 8 and 21 mass percent. The remaining unpolymerized VDMA hydrolyzed to yield NAMA during the emulsion process and was removed during the methanol wash.

Molecular weight data for the PMMA particles are shown in Table 2. The data indicate that the polymer molecular weight and polydispersity index (PDI) were relatively consistent with varying weight percent VDMA. Zero-one theory of emulsion polymerization propagation states that there can be either zero or one radical per polymer particle [16]. This theory generalizes termination events by stating that radical entry into a particle results in simultaneous termination of the existing radical in the particle. In the emulsion system, radical entry into the particles is limited, explaining the large molecular weights that were obtained [16].

FT-IR analysis of polymers demonstrates the presence of hydrolyzed VDMA in the poly(NAMA-*co*-MMA)

Table 2 Characterization data for PMMA particles prepared with varying amounts of initially added VDMA

Polymer	VDMA (Wt. %)[b]	[KPS] (M)	T_g [c] (°C)	M_n^d (kg mol^{-1})	M_w^d (kg mol^{-1})	PDI[d]
V0[a]	0	0.0055	124.9	73.5	287.2	3.9
V1	13	0.0055	121.7	134.7	436.4	3.2
V2	23	0.0054	122.1	171.5	500.7	2.9
V3	32	0.0054	124.7	153.8	445.7	2.9

[a]Particles prepared without the addition of VDMA
[b]Weight percent of VDMA added versus weight of MMA
[c]Determined by DSC using second heating cycle
[d]Determined by GPC

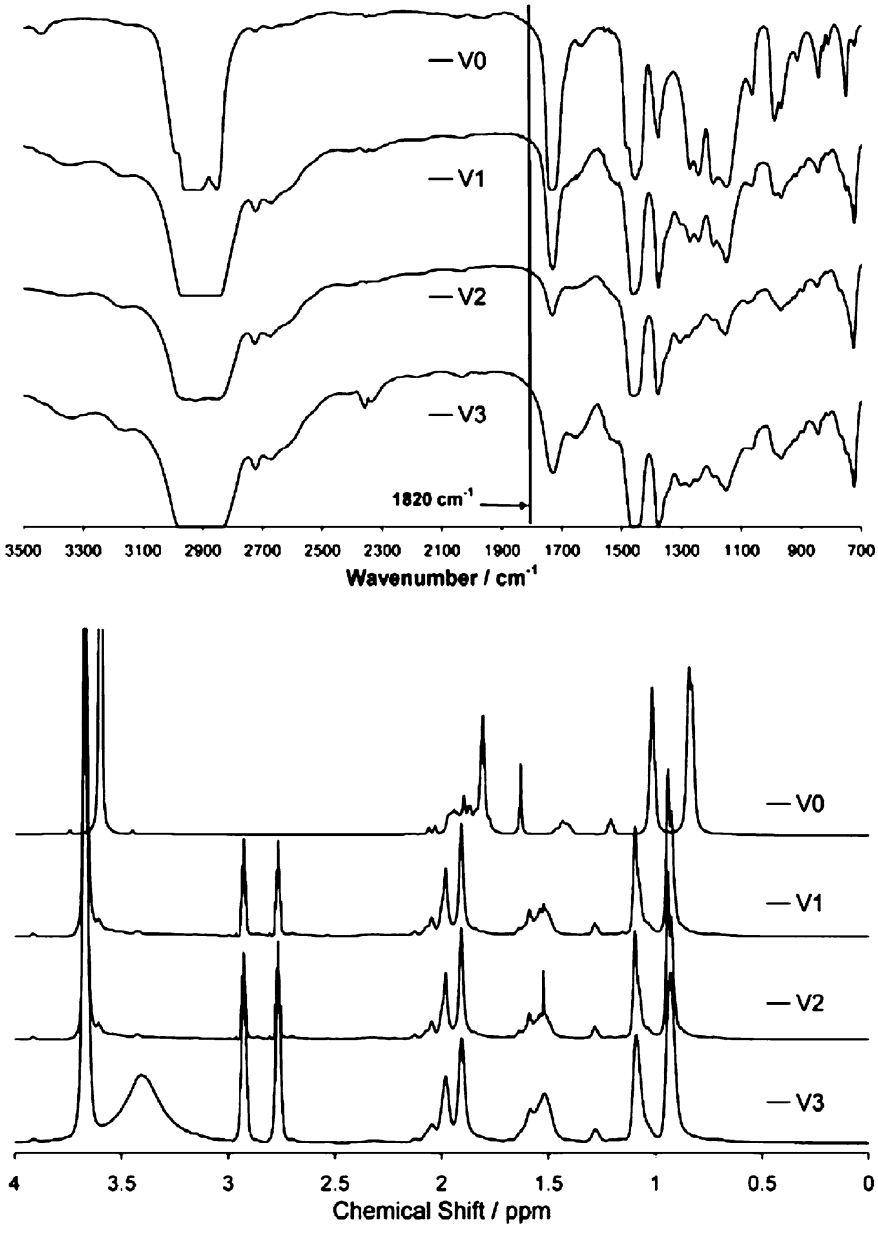


Fig. 4 IR plot of polymers V0–V3 (*top*). ^{1}H-NMR of polymers V0–V3 showing microstructural differences of α-methyl group of MMA between 1.4 and 0.7 ppm (*bottom*)

microspheres. Previously reported FT-IR data of poly-(VDMA) shows a distinct carbonyl absorption (C = O, stretch) at approximately 1,820 cm^{-1} [17]. The IR spectra for polymers V0–V3 are given in Fig. 4 (top), and a peak at 1,820 cm^{-1} was not present in any spectra. However, there are three distinct regions of the plot that indicate NAMA in the polymer. First, at 3,350 cm^{-1}, a broad peak is observed in the spectra of polymers V1–V3, but it is not seen in the spectra of V0. This peak corresponds to N–H stretching vibrations of NAMA. Second, a shoulder is visible to the left of the large peak at 1,750 cm^{-1} for polymers V1–V3. And third, another shoulder is observed in polymers V1–V3 at approximately 1,550 cm^{-1} indicating either N–H stretching or C–N deformation vibrations of NAMA. These peaks are small and not easily defined, but comparison to the spectra of polymer V0 (without added VDMA) and the spectra of NAMA, these peaks clearly illustrates the presence of NAMA in the poly(NAMA-*co*-MMA) microspheres.

Also, proton-NMR (Fig. 4 (bottom) was also used to investigate the presence of NAMA in the poly(NAMA-*co*-MMA) particles. Upon examination of specific regions of the spectra, chemical shifts of the hydrolyzed VDMA can be observed in the spectra of the copolymer particles. Broad peaks at approximate chemical shifts of 7.4 ppm (N–H), 2.4 ppm (main chain CH or CH_2), and

Table 3 Particle size statistics obtained from laser light scattering of polymeric dispersions in methanol

Polymer	[KPS] (M)	Mean particle diameter (μm)	Standard deviation (μm)	Coefficient of variance (%)
K0[a]	0.0055	38.7	22.7	58.5
K1	0.0027	0.594	0.104	15.8
K2	0.0054	0.661	0.134	15.7
K3	0.011	0.712	0.121	18.8
K4	0.015	0.688	0.094	17.6

[a]PMMA prepared without the addition of VDMA as particle stabilizer

1.5 ppm ([$C(CH_3)_2$] and main chain CH or CH_2) are seen in the spectra of polymers V1–V3.

Polymer tacticity is often correlated with physical properties, and ultimately plays an important role in dictating useful applications for a polymeric material, therefore tacticity was examined by proton-NMR and DSC analyses. Proton-NMR spectra were obtained at 80°C in order to improve spectral resolution and specific peaks in the far upfield region of the proton- NMR show tacticity variances of the α-methyl groups of PMMA [18]. In comparison to work done by Shim et al. [18], the tacticity ratios for polymers V0–V3 all corresponded closely to that of more stereoregular syndiotactic PMMA. These peaks, shown in Fig. 4 (bottom), at approximately 1.27, 1.09, and 0.94 ppm, correspond to the syndiotactic (rr), atactic, (mr), and isotactic (mm) triads, respectively, and the ratios of the three can be determined by integration of the peak areas. All of the polymers analyzed show similar integrated areas and therefore similar ratios of rr/mr/mm triads of about 57/38/5.

Typically, commercially available PMMA has 43% syndiotactic triads resulting in a glass transition temperature of approximately 105°C [18]. As shown in the DSC data for the PMMA polymers prepared in this work, the glass transition temperatures were

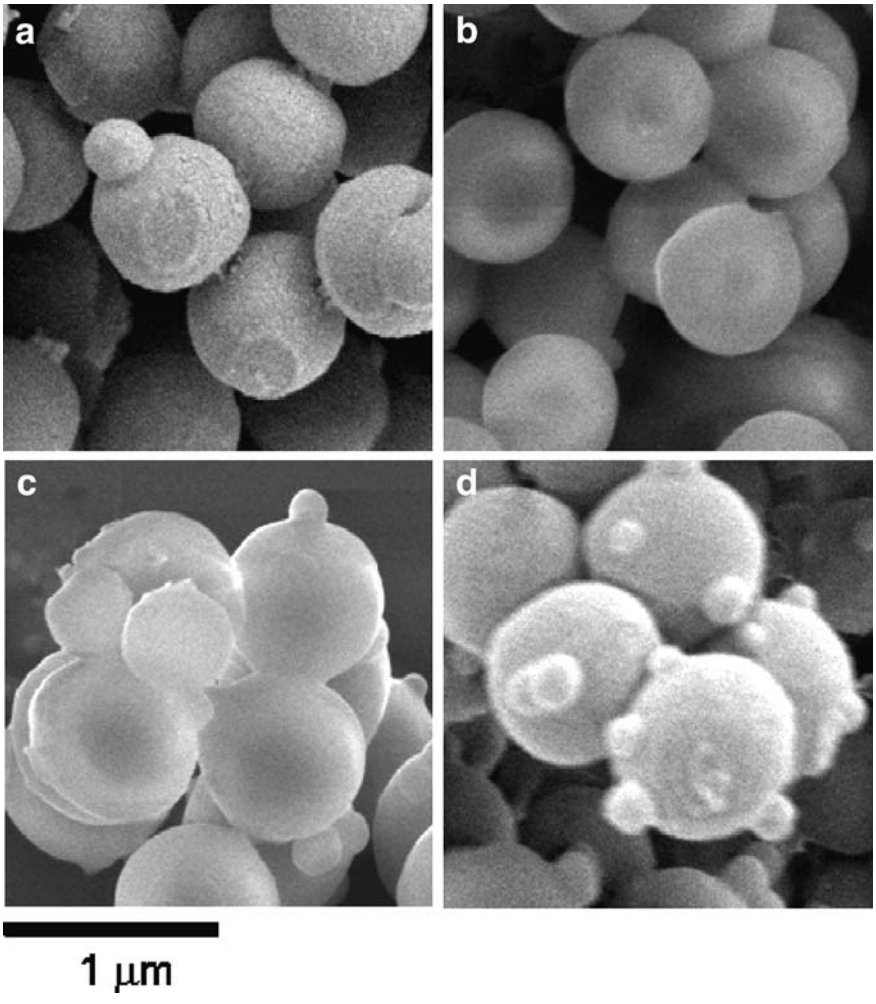


Fig. 5 Representative SEM micrographs of PMMA particles prepared with varying [KPS]: **a** 0.0027 M (K1), **b** 0.0054 M (K2), **c** 0.011 M (K3), **d** 0.015 M (K4)

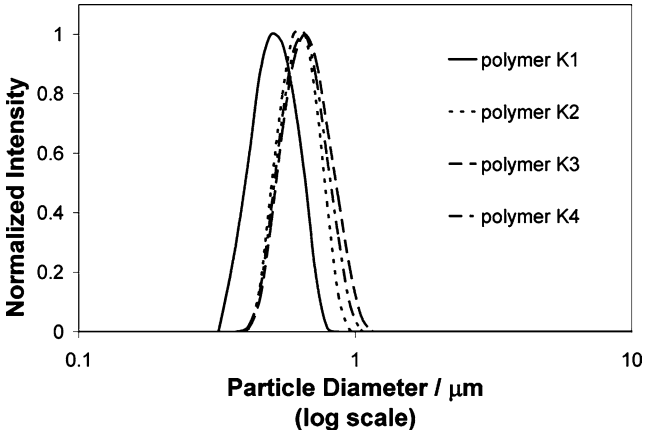


Fig. 6 Plot of normalized differential volume versus particle diameter for copolymers K1–K4

approximately 124°C (see Table 3) which is a direct result of the increased percent of syndiotactic triads (57%) [19]. DSC data also show consistent glass transition temperatures under varying weight fractions of VDMA. Table 3 shows glass transition temperatures that were fairly consistent, between 122 and 125°C, when the weight percent of VDMA was varied from 12 to 32 Wt. %. Additionally, the DSC analysis showed only one glass transistion temperature, indicating a homogenous polymer microstructure.

Varying concentration of potassium persulfate (KPS)

In this section, the preparation of a series of PMMA particles using varied initiator concentration is described. The concentration of initiator, potassium persulfate (KPS) was varied in order to study the effect of initiator concentration on particle size, particle size distribution, and molecular weight. VDMA was added to the emulsion reaction at a constant 32 Wt. % because initial studies described above showed more monodisperse particle sizes and consistent molecular weight using a higher weight fraction of VDMA.

The morphology of the PMMA particles is shown in Fig. 5, and the particles sizes were confirmed by light scattering. The light scattering data indicates particle sizes of less than a micrometer for polymers K1–K4, as shown in Fig. 6 where the concentration of KPS was increased incrementally from 0.0027 to 0.015 M (see Table 3). PMMA particles prepared without the addition of VDMA showed markedly different results. The particle size was nearly 2 orders of magnitude larger for PMMA particles prepared without VDMA. CV values in Table 4 showed relatively good monodispersity for polymers K1-K4, in a range of 15 to 19%, which is considerably better than the particles without added VDMA (K0, 58%). In comparison, polymer K0 had a particle size of 38.4 μm without the addition of VDMA to the emulsion prodecure. With higher initiator concentrations (about 0.071 M KPS) Sivakumar and Rao showed particle sizes of about 14 μm for PMMA particles [15]. In this system, the lower CV values for polymers K1–K4 can be attributed to the stabilization of the particles caused by VDMA copolymerization with MMA followed by hydrolysis to yield poly(NAMA-*co*-MMA).

Molecular weight data for PMMA particles K0–K4 are given in Table 4. The data show decreasing molecular weight when increasing KPS concentration from 0.0055 to 0.010 M (K1–K2). This result is probably due to an increase in the number of polymer particles at higher initiator concentrations [16]. However, as the initiator concentration is further increased in polymers K3 and K4, the molecular weights do not change appreciably. Typically, higher initiator concentrations result in more polymer particles competing for the same amount of monomer. Therefore, less monomer is contained in each particle, limiting the ability for polymer radicals to propagate to higher molecular weight. Although this is the usual observation, in these experiments, the molecular weights for polymers K2–K4 do not show such a trend.

Also, PMMA prepared without added VDMA (polymer K0) had a molecular weight of nearly one-half that of polymers where VDMA was added, and a much

Table 4 Characterization data for PMMA particles prepared varying [KPS]

Polymer	VDMA (Wt. %)[b]	[KPS] (M)	T_g [c] (°C)	M_n^d (kg mol^{-1})	M_w^d (kg mol^{-1})	PDI[d]
K0[a]	0	0.0055	124.9	73.5	287.2	3.9
K1	32	0.0027	122.7	270.1	834.8	3.1
K2	32	0.0054	124.7	153.8	445.7	2.9
K3	32	0.011	122.2	168.7	429.3	2.5
K4	32	0.015	120.7	148.3	347.7	2.3

[a]Particles prepared without the addition of VDMA
[b]Weight percent of VDMA added versus weight of MMA
[c] Determined by DSC using second heating cycle
[d] Determined by GPC

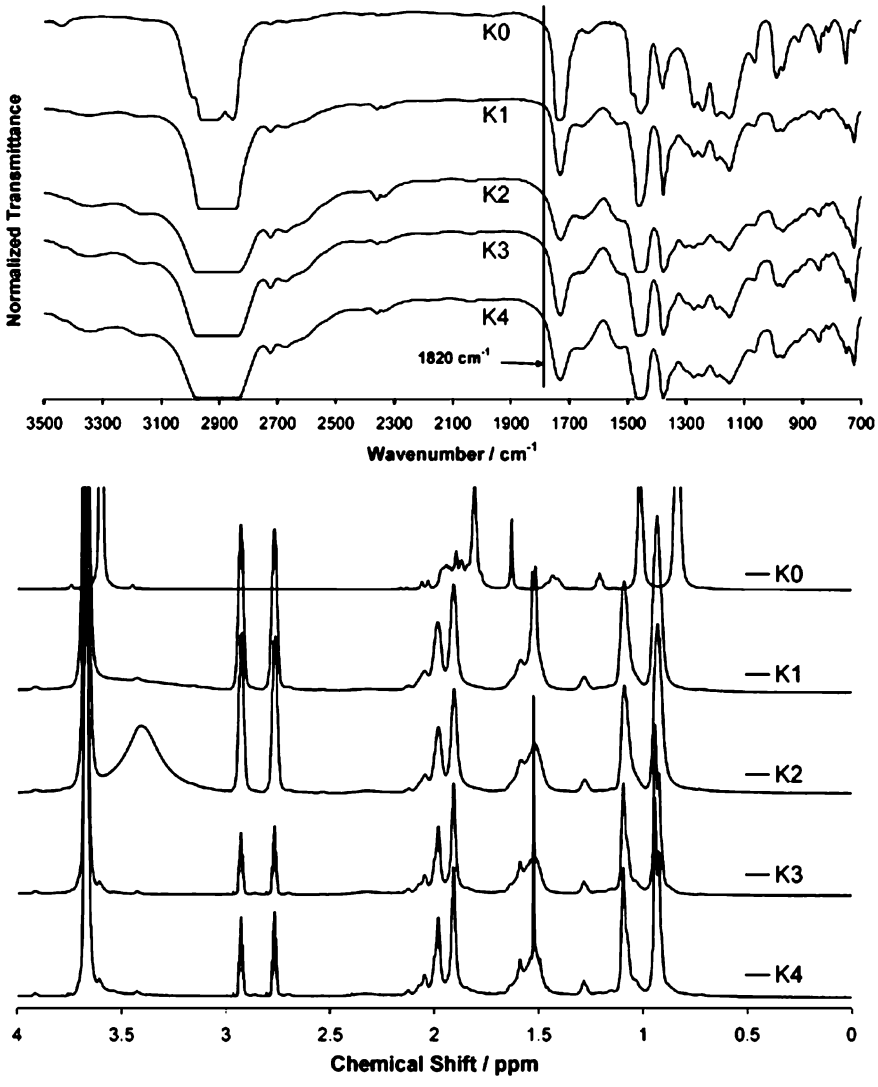


Fig. 7 (TOP) IR plot of polymers K0–K4 (*top*). ^{1}H-NMR of polymers K0–K4 showing microstructural differences of α-methyl group of MMA between 1.4 and 0.7 ppm (*bottom*)

higher PDI. Recent results have shown that high molecular weight PMMA spherical particles can be utilized in bone cement applications [20]. However, the particles were prepared via suspension polymerization and had molecular weights nearly ten times those reported in this work. Usually, the smaller the particle size, the more dispersed the polymer becomes in the cement composition, thus the smaller, uniform, spheres reported here may allow for greater strength of the overall material, and better long-term stability.

The DSC data shown in Table 4 showed one glass-transition temperature, with no significant variation in the T_g with varying concentration of KPS. Therefore, the relatively constant T_g (± 2°C on an average) at about 124°C indicates similar composition of the polymeric microspheres, as seen in Table 4. As stated above, Wang et al. [21] have shown PMMA emulsion particles with glass transition temperatures around 125°C when prepared without a particle stabilizer. Therefore, the increase in the glass transition temperature compared to commercially available PMMA can be attributed to a change in the chemical microstructure of the polymer [18]. The smaller particles seen in Fig. 5 are similar those seen in seeded-emulsion polymerization. In such experiments, multiple glass transition temperatures are often observed, indicating incompatibility of the core and the shell [22]. However, the data shows only one glass transistion temperature for each preparation and it is known from previous work that VDMA and MMA copolymerize randomly in solution [23].

The presence of the NAMA in polymers K0–K4 was determined by performing FT-IR analysis on the polymer particles. The spectra were all similar to those seen in Fig. 4 (top) and show complete hydrolysis of the azlactone ring, and this can be confirmed by the absence of the distinct carbonyl peak at 1,820 cm^{-1} [24].

Additionally, the FT-IR spectra of polymers K1–K4 showed peaks identical to those discussed earlier (Fig. 7).

Proton-NMR spectra also obtained for polymers K0–K4, and were similar to the spectra seen in Fig. 4 (bottom). All of the polymers show similar integrated areas and therefore similar ratios of rr/mr/mm triads of about 57/38/5.

Conclusions

This paper describes the synthesis and characterization of PMMA particles using an emulsion polymerization system where the effects of varying amounts of potassium persulfate (KPS), and 2-vinyl-4,4-dimethylazlactone (VDMA) were examined. It has been found that KPS is an efficient initiator for the polymerization of MMA in the emulsion system, giving consistent molecular weights, average particle sizes, and good coefficients of variance in reactions with constant 32 Wt. % of added VDMA. Additionally, in these preparations, varying amounts of potassium persulfate had no effect on the particle size and size distribution, molecular weight and PDI, and glass transistion temperature. Evidence in this paper demonstrates that the addition of VDMA results in copolymerization with MMA followed by water hydrolysis, which yields an NAMA containing polymer particle. The presence of NAMA stabilzes the polymer particles resulting in narrow particle size distribution. However, the addition of VDMA in varying amounts had little effect on the molecular weight of the polymer. The ability to prepare monodisperse microspheres in the sub-micron size range has prospects in a number of applications where narrow particle size distributions and consistent molecular weights are of importance. These particles also show promise for immobilization applications where the presence of carboxyl functionality for covalent attachment is a convenient site for further polymer modification.

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References

1. Ratner BD, Hoffman AS, Schoen FJ, Lemons JE (1996) Biomaterials science: an introduction to materials in medicine. Academic, San Diego
2. Raghuvanshi RS, Katare YK, Lalwani K, Ali MM, Singh O Panda AK (2002) Int J Pharm 245:109
3. Kwon H-Y, Lee J-Y, Choi S-W, Jang Y Kim J-H (2001) Colloids Surf A 182:123
4. Song C, Labhasetwar V, Cui X, Underwood T Levy RJ (1998) J Controlled Release 54:201
5. Kuhn K-D (2000) Bone cements. Springer, Berlin Heidelberg New York
6. Fujita H, Ido K, Matsuda Y, Iida H, Oka M, Kitamura Y Nakamura T (2000) J Biomed Mater Res 49:273
7. Lee JS, Nam YS, Kang B-Y, Han S-H Chang IS (2004) J Appl Polym Sci 92:517. DOI: 10.1002/app.20028
8. Tzoris A, Hall EAH, Besselink GAJ Bergveld T (2003) Anal Lett 36:1781. DOI: 10.1081/AL-120023614
9. Sivakumar M, Rao KP (2002) J Biomater Sci Polymer Ed 13:111. DOI: 10.1163/156856202317414311
10. Tao SL, Lubeley MW, Desai TA (2003) J Control Release 88:215. DOI:10.1016/S0168-3659(03)00005-1
11. Tao SL, Lubeley MW, Desai TA (2003) J Biomed Mater Res 67A:369. DOI: 10.1002/jbm.a.10047
12. Dufour MG, Guyot A (2003) Colloid Polym Sci 281:105. DOI: 10.1007/s00396-002-0752-6
13. Boisson F, Uzulina I, Guyot A (2001) Macromol Rapid Comm 22:1135
14. Aramendia E, Barandiaran MJ, Asua JM (2003) C R Chim 6:1313
15. Sivakumar M, Rao KP (2000) React Funct Polym 46:29
16. Gilbert RG (1995) Emulsion polymerization: a mechanistic approach. Academic, London
17. Drtina GJ, Heilmann SM, Moren DM, Rasmussen JK, Krepski LR, Smith HK II, Pranis RA Turek TC (1996) Macromolecules 29:4486. DOI: 10.1021/ma9517310
18. Shim SE, Shin Y, Jun JW, Lee K, Jung H, Choe S (2003) Macromolecules 36:7994. DOI: 10.1021/ma034331i
19. Brandup J, Immergut EH (1975) Polymer handbook, 2 Edn. Wiley, New York
20. Shinzato S, Nakamura T, Kawanabe KTK (2004) J Biomed Mater Res Part B: Appl Biomater 68B:132. DOI: 10.1002/jbm.b.20008
21. Wang D, Luo Q, Xiaodong L, X. W, Yong H, Zhen Z, Liu X Jia D (2003) Colloid Polym Sci 282:48. DOI: 10.1007/s00396-003-0912-3
22. Wang G, Wang X, Jin R (2004) Colloid Polym Sci 283:98
23. Stanek LG, Heilmann SM, Gleason WB (2003) J Polym Sci A Polym Chem 41:3027
24. Heilmann SM, Rasmussen JK, Krepski LR (2001) J Polym Sci A Polym Chem 39:3655