Preparation and Characterization of pH-Sensitive Microgels of Poly((2-dimethylamino) ethyl methacrylate)

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Summary: pH-sensitive microgels of poly((2-dimethylamino) ethyl methacrylate) (PDMAEMA) were prepared by dispersion polymerization of 2-dimethylamino ethyl methacrylate in a mixed solvent of water/ethanol. ^{1}HNMR, FTIR and SEM were used to confirm the chemical structure and morphological properties of the resulting microgels. Dynamic Light Scattering (DLS) was used to measure the hydrodynamic diameter of the particles. SEM micrographs showed that the microgel particles have a diameter of about 100–200 nm in dry state. Mean hydrodynamic diameter of the particles at their collapsed state at $pH = 9.5$ was found to be about 150 nm. DLS measurements at various pH values showed that the prepared microgels have a volume phase transition around $pH = 8$ at which the hydrodynamic diameter decreased from about 470 nm to around 150 nm corresponding to a 32 fold change in the mean volume of a microgel particle.

Keywords: dispersion polymerisation; microgels; nanoparticles; pH-Sensitive polymers; poly((2-dimethylamino) ethyl methacrylate)

Introduction

Colloidal microgels may be defined as intramolecularly crosslinked polymeric particles usually dispersed in an aqueous solvent, displaying hydrodynamic diameters in the range of ~100 nm to 1 μm.[1] Depending on its degree of crosslinking, and on the nature of the solvent, the microgel will be more or less swollen. If an environmentally-sensitive polymer is used in the preparation of the microgel particles, they can be expected to have similar responsive properties to that of their linear counterpart. In recent years, increasing attention has been paid to the synthesis and applications of stimulus-responsive microgels[1–6] among which, pH- and/or temperature-sensitive microgels are probably the most extensively studied classes. Essentially every property (e.g. particle size, viscosity, etc.) of these sub micrometer gel particles changes when the physicochemical conditions of the aqueous environment surrounding them is changed to bring about a phase transition in the network.[2,7,8] These interesting materials are being investigated for various applications such as drug delivery,[9] separation of proteins,[3] optics,[6] removal of heavy metal ions,[10] catalysis[11] and rheological control.[8]

Although there have been extensive studies on microgels with acidic groups (e.g. methacrylic acid), there are few reports on cationic microgels. Recently, cationic microgels have received considerable attention primarily because of their potential for biomedical applications.[1,4,7] Poly((2-dimethylamino) ethyl methacrylate) (PDMAEMA) is a cationic polyelectrolyte which has been shown to be sensitive to both pH and temperature[12–14] and has been

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used in various biomedical applications such as gene delivery[15] and glucose-sensitive controlled release systems.[16] To the best of our knowledge, there hasn't been any report on the preparation and pH-sensitive characteristics of PDMAEMA microgels. Herein we report on the synthesis and characterization of PDMAEMA microgels by a simple single-step dispersion polymerization method in aqueous media and their pH-sensitive swelling behavior in buffer solutions of various pH

Materials and Methods

Materials

The monomer (2-dimethylamino) ethyl methacrylate (DMAEMA) (Merck) was passed through a column of basic alumina to remove inhibitor. α, α'-azodiisobutyramidine dihydrochloride (V-50) (Sigma), N,N′- Methylenebisacrylamide (BIS) and ethanol (Merck,Germany) were selected as initiator, crosslinking agent, and cosolvent respectively and used as received. Deionized water was used in all experiments.

Microgel Synthesis

A free-radical dispersion polymerization method was used to prepare the microgel particles. The polymerizations were conducted in a 250 mL, four-necked flask fitted with a poly(tetrafluoroethylene) (PTFE) anchor-shaped mechanical stirrer, a condenser, a thermometer and a nitrogen inlet and outlet. 84.4 mL of deionized water was placed in the reaction vessel, which was immersed in a water bath set at 65 °C. Nitrogen was bubbled through the solution which was stirred for 30 minutes at 200 rpm. 25.9 mg of BIS was added to the solution and five minutes later, 5.285 g of DMAEMA dissolved in 5 mL of nitrogen purged ethanol was added to the reaction solution. After one minute, the polymerization was started by adding 10.6 mL of a previously nitrogen purged solution of V-50 (5 mg mL^{-1}) dissolved in deionized water. Thirty seconds later opalescence appeared and the reaction was continued for 6 hours. After cooling the resultant mixture, serum replacement (ultrafiltration)[17] was used to eliminate ethanol, linear polymer and any traces of unreacted monomer and initiator, to purify the PDMAEMA microgels. Ultrafiltration was performed using a Sartorius stirred cell ultrafiltration device (Sartorius AG, Germany) by replacing the serum with water; this serum was periodically collected to assess the extent of purification. Purification was continued until the serum conductivity was close to that of the employed water (5–7 μS cm^{-1}). A portion of the final purified microgel dispersion was freeze-dried and kept at $-60\,^{\circ}$C for later use.

Measurements

At certain time intervals, 0.5 mL samples were withdrawn from the polymerization vessel and cooled in an ice bath for kinetic measurements. These samples were dried in a vacuum oven at room temperature and then used to calculate the monomer conversion by a gravimetric method.

^{1}HNMR spectra of unpurified microgel dispersions were recorded on a JEOL JNM-EX90A spectrometer. A small amount of the unpurified latex was cast onto a Petri dish and dried in vacuum oven at room temperature. The resultant dried film was dissolved in $CDCl_3$ and ^{1}HNMR spectra were recorded at ambient temperature. The chemical structure of the purified microgel was characterized by FTIR spectroscopy using the KBr method. A small amount of the freeze-dried microgel was dissolved in chloroform and a drop of this solution was placed on a KBr pellet and then dried in vacuum. FTIR spectra were recorded on a BioRAD FTS-7 spetrometer.

Scanning Electron Microscopy (SEM) was used to characterize the morphology of microgels in the dry state. To prepare scanning electron microgaphs of the nanoparticles, freeze-dried microgel particles were dispersed in ethanol, stirred for 24 hours and sonicated for 15 minutes. A drop of the resultant dispersion was placed on a SEM stub, freeze-dried and then sputter-coated with a thin layer of gold prior to inspection with a Philips XL30 (Philips, The Netherlands) scanning electron microscope.

Equilibrium swelling studies were performed to characterize the pH-responsive behavior of the PDMAEMA microgels. To determine the equilibrium swelling behavior, purified microgel dispersions were diluted with buffer solutions to a concentration of 0.2 mg mL^{-1} of polymer, assuming complete conversion of the monomer. Acetate buffer was used for pH 3 and 4; phosphate buffer for pH 6, 7 and 8 and borate buffer for pH 9.5. The ionic strength was kept constant for all solutions at $I = 0.075$ mM by adding appropriate amounts of sodium chloride (Merck) to each solution. The samples were left to equilibrate for one hour before sizing. Hydrodynamic particle diameters were measured at 27 °C using a SEMATech 630 (SEMATech, France) instrument fitted with a He-Ne laser ($\lambda = 632.8$) with a detector at 90°.

Results and Discussion

The esteric bond in the DMAEMA monomer is very susceptible to hydrolysis in water but unlike its monomer, PDMAEMA is quite stable toward hydrolytic degradation even at very unfavorable conditions.[18,19] Using the information provided in van de Wetering et al.,[19] it can be estimated that less than 1% of the monomer will be hydrolyzed after one minute in the reaction conditions reported here. The results of ^{1}HNMR analyses of the unpurified latex are illustrated in Figure 1. There are no characteristic carboxylic acid peaks around $\delta = 11.5$ ppm which is an indication of the absence of any hydrolytic degradation of monomer.

Figure 2 shows the FTIR spectrum of the purified microgel dispersion, which along with the results of ^{1}HNMR, confirms the successful synthesis of the polymer with the intended chemical structure. The following characteristic peaks can be observed in the spectrum (cm^{-1}): 1735, carbonyl stretch vibration; 2920–2960, N-$(CH_3)_2$ stretch vibration; 1162, C-O-C carbonyl stretch vibration; around 1476, N-$(CH_3)_2$ deformational stretch vibration. Previous studies have shown that hydrogels of poly(N-isopropylacrylamide),[20] its copolymers[21] and also poly(acrylamide) contain some amount (~10–20%) of bounded water even after several months of drying under vacuum.

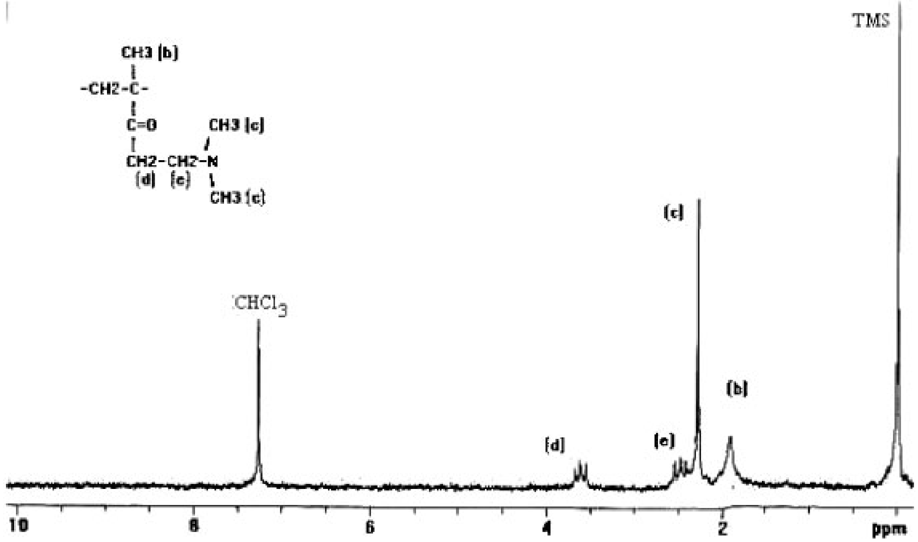

Figure 1.
^{1}HNMR spectrum of the unpurified microgel dispersion (microgel particles and linear polymer).

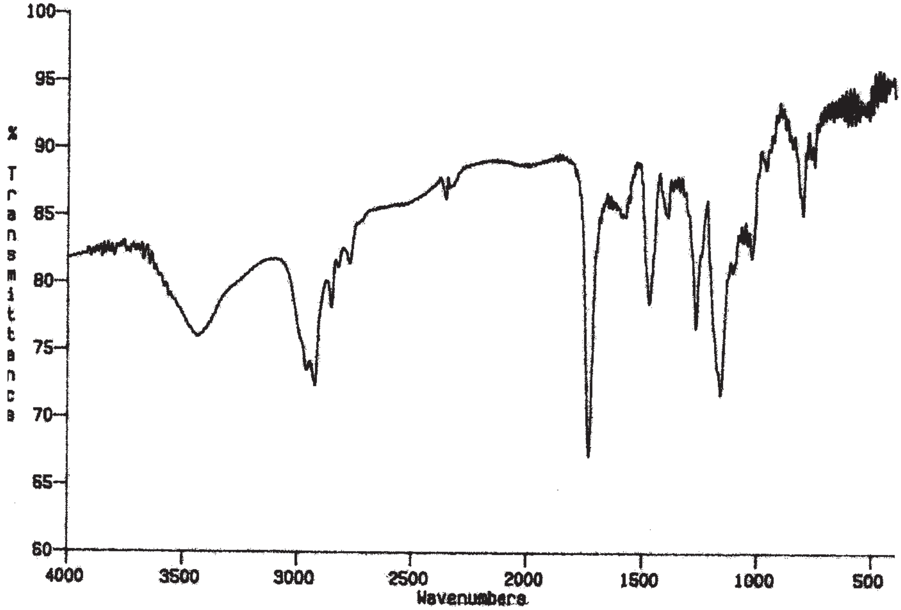

Figure 2.
FTIR spectrum of purified PDMAEMA microgel particles.

Therefore the broad peak around 3300–3450 cm^{-1} may be attributed to the bound water in the network structure of the microgels.

Figure 3 shows the conversion of DMAEMA against time. As can be seen, the reaction proceeds very fast and reaches ~80% conversion in about 30 minutes. One of the characteristic features of dispersion polymerization is its very fast reaction kinetics.[22] For example, in the dispersion polymerization of N-isopropylacrylamide

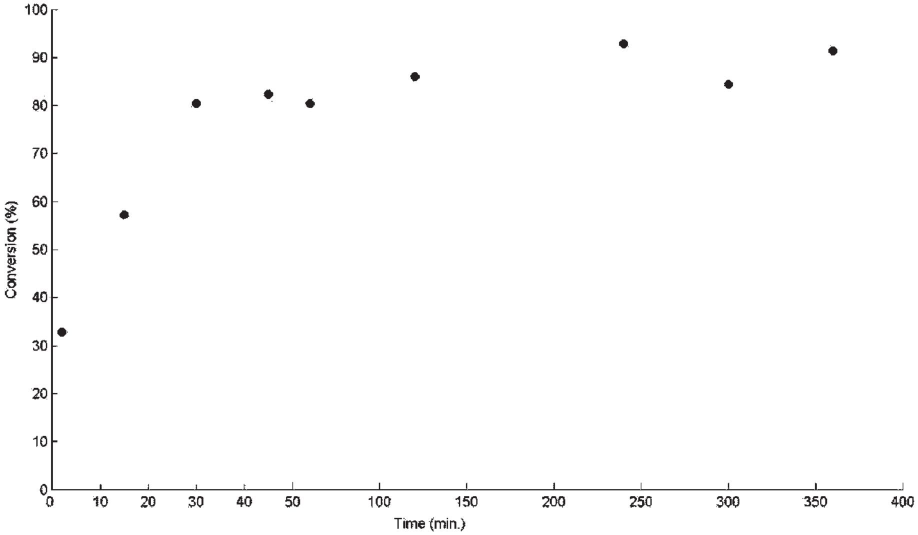

Figure 3.
DMAEMA conversion versus the reaction time.

(NIPAAm) to prepare PNIPAAm microgels; conversion reaches a value of around 80% in about 13 minutes at 70 °C.[23] This high rate of polymerization has been attributed to the increased viscosity inside monomer-polymer particles and the concomitant reduction in the termination rate of radicals inside the particles (the gel effect).[22,24]

Figure 4 illustrates a sample SEM micrograph of the produced microgel particles. It has to be noted that due to the low glass transition temperature (T_g of the analogous linear polymer is 19 °C) and rubbery nature of PDMAEMA microgels, preparing SEM micrographs of these materials is somewhat problematic.[4] We tried to prepare SEM micrographs from microgel dispersions in water at both acidic and basic media, but the resultant SEM micrographs contained large amounts of coagulations. According to previous findings, ethanol is a better solvent for PDMAEMA than water,[25] which means a better match of the Hamaker constants between microgel particles and ethanol resulting in better stability of nanoparticles toward coagulation.[22] This was indeed the case for SEM micrographs prepared from microgel dispersions in ethanol. As is shown in Figure 4, the dry-state diameter of the microgels is about 100–200 nm and considering that these microgel particles are not stabilized by any kind of colloidal stabilizer, the amount of coagulation present is fairly small.

DLS experiments were used to measure the hydrodynamic diameter of the prepared nanoparticles at different pH values. Figure 5(a) shows the particle size distribution of microgel particles at pH 6 and ionic strength $I = 0.075$ mM. As can be seen, although no effort has been made to optimize the polymerization recipe, the size distribution of the microgel particles is fairly narrow. This can be attributed to the inherent mechanism of the dispersion polymerization in which it is possible to prepare dispersions with very narrow size distributions with a simple process.[26,27] The small peak above 1 μm may be due to flocculation. The results of equilibrium swelling measurements are presented in Figure 5(b). The error bars represent standard errors ($n = 3$). As can be seen, increasing the pH of the surrounding medium leads to a sharp decrease in the hydrodynamic diameter of the Microgels from ~470 nm to ~150 nm at a pH of about 8. In acidic media, the tertiary amine side chains of the DMA residues become protonated, thus increasing the charge density on the network.

The concomitant increase in mobile counterion content of the network with the corresponding increase of internal osmotic pressure[14] accompanied with charge repulsion between neighboring amine groups,[28]

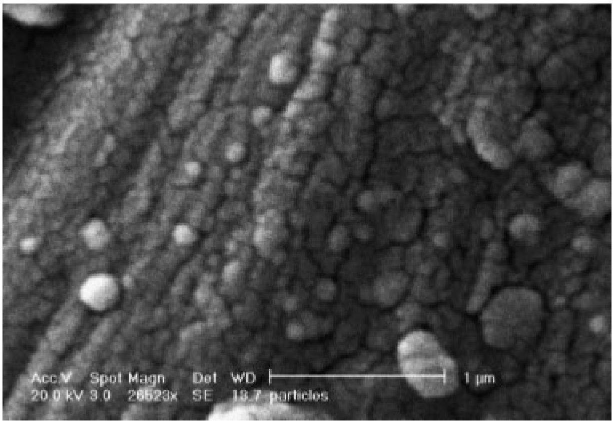

Figure 4.
Sample SEM micrograph of dried PDMAEMA microgel particles.

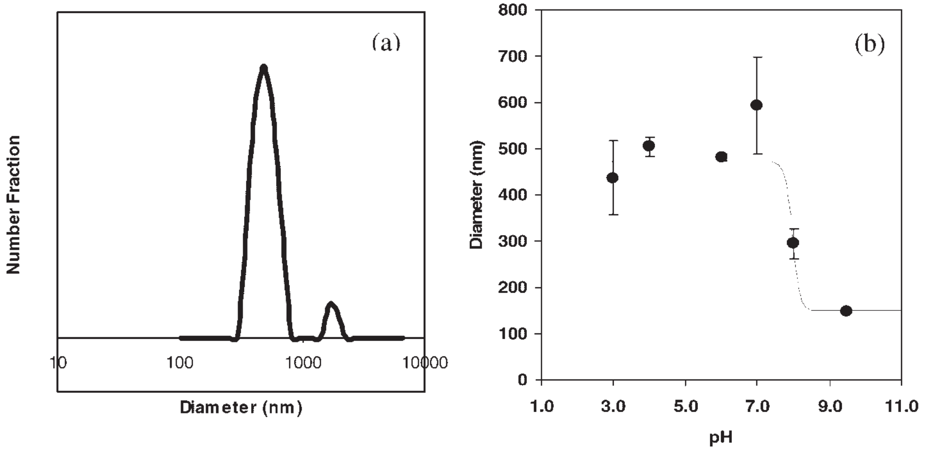

Figure 5.
Results of DLS measurements on microgel particles (a) particle size distribution of the latex at pH = 6 and ionic strength of $I = 0.075$ mM; (b) variation of the average hydrodynamic diameter of the microgel particles with pH. The solid line in (b) is a guide to the eye rather than a fit to the data.

leads to the observed swelling transition. The degree of microgel character is reflected in the volumetric swelling factor, i.e., the cube of the ratio of the microgel diameter at pH = 3 to that of the microgel diameter at alkaline pH.[4] Swelling factors greater than 10 indicate good microgel character and for this microgel it is nearly 32 which may be compared to similar cases reported in the literature.[4]

Conclusions

A simple dispersion polymerization method was employed to synthesize pH-sensitive microgel particles of PDMAEMA. FTIR and ^{1}HNMR analyses were used to confirm the chemical structure of the microgel. SEM micrographs showed that the nanoparticles have a diameter of ~100–200 nm in their dry state. Dynamic light scattering of the microgel dispersions in different pH values demonstrated the pH-responsiveness of the microgel particles. The results showed that the microgels have a pH-sensitive phase transition around pH 8 where the mean microgel particle diameter changes from ~470 nm to ~150 nm. Application of these microgels as actuators in membranes for drug delivery is currently under investigation in our laboratory.

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