Synthesis and Characterization of Poly (N-Ethylmethacrylamide) Thermosensitive Latex Particles

P. Hazot[1], Th. Delair[1], A. Elaissari[1], C. Pichot*[1], J. P. Chapel[2], J. Davenas[2]

1)UMR-103, CNRS-bioMérieux, ENS de Lyon, 46 allée d'Italie, 69364 Lyon Cedex - France
2)UMR-5627, LMPB, UCBL1, 43 Bd. du 11 Nov. 1918, 69622 Villeurbanne Cedex - France

SUMMARY : Thermosensitive crosslinked polymer latexes exhibiting high "Volume phase transition temperature" (T_{VPT}) have been prepared by a batch precipitation polymerization process using N-ethylmethacrylamide (NEMAM) as main monomer, ethylene glycol dimethacrylate (EGDMA) as a crosslinker and potassium persulfate (KPS) as the initiator. The effect of KPS on the water soluble polymer formation and on the final particle size of the prepared microgel particles was investigated and discussed. The thermosensitivity of the final particles was revealed both by particle size analysis using QELS (Quasi-elastic light scattering) and optical density as a function of temperature. In addition, the swelling ability of the prepared microgels reflected the cross-link density of the particles.

Introduction

A hydrogel microsphere (microgel) is expected to find its applications in various fields including as a solid phase support to immobilize biomolecules1), as drug delivery system (DDS)2), as coating technology etc., because of its quick environmental response. For instance, polyacrylamide and its N-substitued polymers have attracted much interest due to their unique thermal response in aqueous medium3). Studies on aqueous solutions of poly(N-isopropylacrylamide) show that the phase transition takes place reversibly as a function of temperature and almost independently of molecular weight and concentration4). The phase transition temperature of this series of N-substitued polyacrylamide derivatives strictly differs depending on the chemical structure of the side chains5).

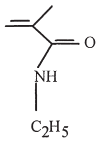
The purpose of this work is to investigate the preparation of monodisperse thermosensitive microgel poly(NEMAM) particles exhibiting higher T_{VPT} than those of poly(N-isopropylacrylamide) (T_{VPT}~32°C) and poly(N-isopropylmethacryalmide) (T_{VPT}~43°C).

CCC 1022-1360/00/$ 17.50+.50/0

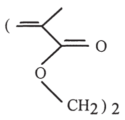
Particular attention was paid to the effect of potassium persulfate (KPS) initiator on polymer conversion, water soluble polymer formation, hydrodynamic particle size, size distribution, swelling ratio and T_{VPT}.

Experimental Section

Synthesis of Poly(NEMAM) particles : Microspheres were prepared by batch polymerization using NEMAM (1g) as a principal monomer, EGDMA (0.15g) as a crosslinker and KPS (from 0.01 to 0.06g) as an initiator. The polymerization was carried out at 90°C in 50 ml boiled and deoxygenated water as a total volume. After 6 hours of polymerization reaction, the final conversions were determined. The final latexes were centrifuged in order to determine the water soluble polymer content.



NEMAM



EGDMA

Characterization of Latexes : The polymer conversions and the water soluble polymer content (pooled after centrifugation step) were gravimetrically determined from which the particle yield was deduced. Particle size was measured both by QELS (Quasi-Elastic Light Scattering) and SEM (Scanning Electron Microscopy). The polymer conversions versus time were determined by ^{1}H NMR. The T_{VPT} of the prepared thermosensitive particles (diluted in 10^{-3}M NaCl) was determined by measuring the optical density (OD) variation as a function of temperature.

Results and discussion

Conversion and particle size : All the latexes reached relatively high conversions (>80%) corresponding to both polymer particles and water soluble polymer. The conversion versus time curves are reported in Fig 1, showing that the polymerizations are almost completed within 60 min and 120 min for 0.06 and 0.01g of initiator respectively. It is worth noting that QELS size (measured at 20°C, 10^{-3} M NaCl) versus polymerization time was found to in the investigated range (see Fig 2). This behavior can be attributed to a constant particle number established early in the reaction under such conditions, which explains the production of a monodisperse latex particles as evidenced from scanning electron micrographs (SEM) as reported in Fig 3. It seems that, the influence of initiator is operating not only to accelerate the precursor particles production (as reflected by conversion vs. time, see Fig1) but also on the growth of mature particles as evidenced from Fig 2, in which the final particle size seems to be KPS concentration dependent. In fact, the larger the concentration of initiator, the smaller the final particle size (measured at 20°C). The opposite trend was observed in the case of N-isopropylmethacrylamide (NIPMAM)/ methylenebisacrylamide (MBA) system$^{6)}$. This phenomenon reflects that poly(NEMAM) chains induce more efficient stabilization to compensate the ionic strength effect originated from the initiator concentration.

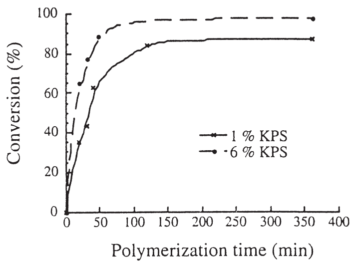


Fig.1: Conversion versus time as a function of initiator concentration (1 and 6% w/w).

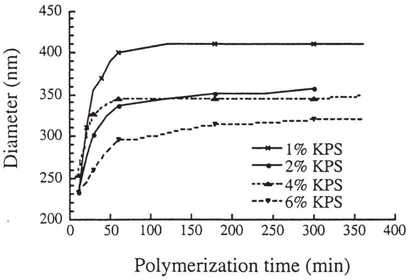
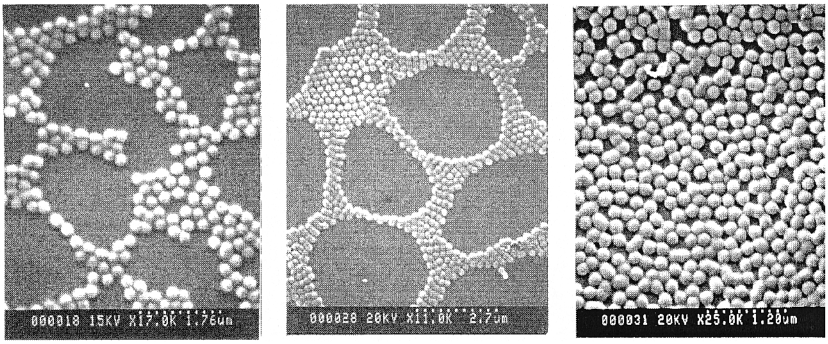


Fig.2: Effect of KPS on particle size (at 20°C) versus polymerization time

Water soluble polymer : Increasing the initiator concentration significantly enhanced the formation of water soluble polymer, as reported in Fig 4. This may be attributed to the combination of rapid consumption of EGDMA crosslinker and to the production of short oligomer chain length with increasing the KPS concentration in the polymerization recipe. In addition, the high initiator rate decomposition (kd>7.10^{-5} s^{-1} at 90°C) at such polymerization temperature favors the formation of high WSP content, since a polymerization temperature effect was reported in the case of NIPMAM polymerization using MBA as a cross-linker$^{6)}$: the higher the temperature, the greater the WSP formation.



1 % KPS 2 % KPS 6 % KPS

Fig.3 : SEM micrographs of poly(NEMAM) microgel particles as a function of initiator concentration (The mass ratio % w/w refers to NEMAM monomer).

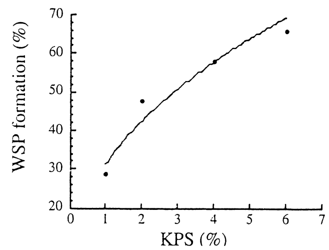


Fig. 4 : Effect of KPS concentration on water soluble polymer formation.

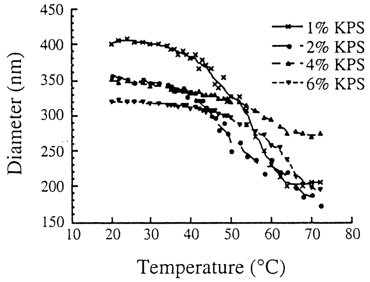


Fig. 5: Average particle diameters as a function of temperature. Effect of KPS.

Latex properties: The obtained latexes were first cleaned several times in order to remove all formed water soluble polymer before any colloidal characterization. As illustrated in Fig. 5, in which the average particle diameters versus temperature (at 10^{-3} M NaCl) exhibit the well known transition of coil to globule conformation of thermosensitive polymers with a decrease in particle size in a broad range of temperature (between 50 to 65°C corresponding to the T_{VPT} domain of microspheres of poly(NEMAM)). Therefore, the particle swelling7) ratio (SR) was determined from the ratio of the particle volume at 20°C to the volume provided by SEM measurement (i.e., $SR=(D_{20°C}/D_{SEM})^3$) which directly reflects the structure of the prepared particles (i.e. the cross-link density of the particle) versus polymerization recipe. As shown in Fig. 6, the swelling ratio decreased when the KPS concentration was increased. This behavior can be attributed to the crosslinker incorporated amount in the final particles reflecting that small particles prepared at high initiator concentration are more cross-linked that large particles. In fact, the increase in initiator concentration leads to the formation of short poly(NEMAM) chains length between knots causing a restriction of the chain mobility within the particles.

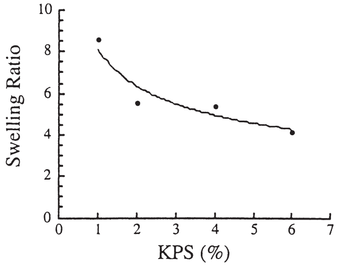


Fig. 6 : Swelling ratio of poly(NEMAM) particles as a function of KPS concentration.

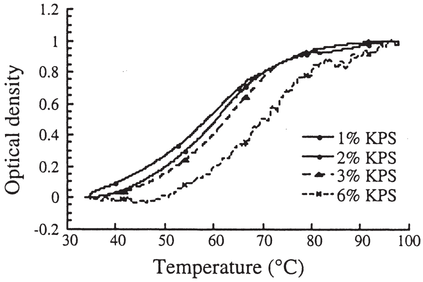


Figure 7: Optical density (OD) at 500 nm wavelength versus temperature for different KPS concentrations.

If no flocculation occured, the T_{VPT} can be determined from the inflection of the OD versus temperature (Fig. 7) at a given ionic strength for stable dispersion. The effect of initiator on T_{VPT} was only significant for the highest KPS concentration (6 % KPS). In order to confirm the observed behavior (T_{VPT} versus initiator amount) complementary techniques are needed such as Differential Scanning Calorimetry and Fluorescence.

Conclusion

Thermosensitive microgel particles were prepared using batch precipitation polymerization in water of N-ethylmethacrylamide (NEMAM), ethylene glycol dimethacrylate (EGDMA) and potassium persulfate (KPS) at 90°C. High conversions (>80%) together with rapid polymerization rates were obtained irrespective of initiator concentrations in the investigated range. Water soluble polymer formation and swelling ratio were controlled by KPS concentrations. In fact, the increase in initiator induces an increase in water soluble polymer formation. High swelling ability of the microgel was obtained for low initiator concentration.

concentrations. In fact, the increase in initiator induces an increase in water soluble polymer formation. High swelling ability of the microgel was obtained for low initiator concentration. QELS particle size versus temperature reflected the thermosensitivity of the prepared monosized latex particles.

Based on this preliminary study, poly(NEMAM) microgel latex preparations are currently investigated in order to point out the effect of EGDMA cross-linker on the polymerization mechanism and on the latex properties.

References

1. H. Kawaguchi, Microspheres, Microcapsules and Liposomes,Vol.1:Preparation and chemical applications, Reza Arshady Editor, Citus reference series, Imperial College of Science, Technology and Medicine, University of London, p.237, 1999.
2. C. Chavany, T. Le Doan, P. Couvreur, F. Puisieux, C. Hélène, *Pharmaceutical research*, **9**, 441, 1992.
3. S. Fujishige, S. Ito, « Chromic Materials and Its Applications », K. Ichimura, Ed., CMC Tokyo, 1989.
4. S. Fujishige, K. Kubota, I. Ando, *J. Phys. Chem.*, **93**, 3311, 1989.
5. S. Itoh, *Koubunshi Ronbunshu*, **46**, 427, 1989.
6. D. Duracher, A. Elaïssari , C. Pichot , *J. Polym. Sci, Part A: Polym. Chem.*, **37**, 1823, 1999.
7. M. Sen, O. Güven, *J. Polym. Sci., Part B, Polym. Physics*, **36**, n°2, 213, 1998.
8. X. Wu, R. H Pelton, A.E Hamielec, D.R. Woods, W. Mc Phee, *Colloid. Polym. Sci.*, **272**, 467, 1994..