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Optimized buffered polymerizations to produce *N*-vinylcaprolactam-based microgels

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ABSTRACT

Temperature-sensitive *N*-vinylcaprolactam (VCL)-based microgel particles were synthesized by emulsion polymerization in a batch reactor. To avoid the hydrolysis of VCL, optimized buffered reactions were carried out by using VCL as main monomer, *N*,*N*′-methylenebisacrylamide (BA) as cross-linker and a sugar-based comonomer (3-*O*-methacryloyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, 3-MDG). The amounts of initiator, cross-linker, surfactant, comonomer, and reaction temperature were the reaction variables. The effects of these variables on the kinetic features of the different polymerizations were analyzed. The colloidal characterization of the microgel particles consists of the analysis of the evolution of the average hydrodynamic diameters as a function of the temperature of the medium. The results showed that in all cases BA reacted faster than VCL. All final microgel particles showed swelling-de-swelling behavior by changing the temperature of the medium in which they are dispersed. Initially formed microgel particles were not temperature-sensitive being necessary up to about 30% of VCL conversion for the onset of the swelling-de-swelling behavior. The final colloidal characteristics of these new microgels can be tuned by modulating the reaction variables.

1. Introduction

Colloidal microgels became an important subdivision of polymer colloids and numerous synthetic microgel systems have been developed to the moment. Their distinct property is the ability to swell in a thermodynamically good solvent and they are prevented from dissolving due to their chemically or physically cross-linked network. The broad range of applications of microgels arises from their stimulus-responsive nature, that is, their ability to undergo reversible volume phase transitions in response to environmental stimuli [1]. Among microgels, those made of thermoresponsive polymers that exhibit lower critical solution temperatures (LCSTs) in aqueous media have received particular attention, given the wide range of applications of materials that respond reversibly to temperature changes [2]. For example, poly(*N*-vinylcaprolactam) (PVCL) [3–7] belongs to a class of biocompatible polymers [8] which undergo a transition from the hydrophilic to hydrophobic state with increasing the temperature. The response mechanism of microgel particles is dictated primarily by the chemical composition, surface charge, morphology and size, and those properties depend strongly on the main reaction variables (temperature, concentration and type of initiator, surfactant, and monomers).

The synthesis of new microgel systems with tailored properties is still a big challenge and for example, recently there is a growing interest in modulating the phase transition critical temperatures of the microgels by adding a more hydrophilic and/or a more hydrophobic comonomer in the recipes. One type of hydrophobic biocompatible monomer is the sugar-based monomer 3-*O*-methacryloyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3-MDG) [9]. Many authors have investigated different polymeric systems based on 3-MDG. Muthukrishnan et al. [10,11]

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synthesized surface-grafted hyperbranched glycopolymers by using 3-MDG as a sugar-carrying monomer. Wulff et al. [12] copolymerized vinyl sugar units with styrene, methyl methacrylate, and acrylonitrile in solution and in bulk [13]. Ohno et al. synthesized block copolymers type polystyrene-*b*-poly(3-MDG) [14] by atom transfer radical polymerization (ATRP). Koch et al. [15] and Al-Bagoury et al. [16] investigated the batch and semi-continuous emulsion copolymerization of 3-MDG and butyl acrylate. However, to the best of our knowledge, in the literature there is not any report on the synthesis of 3-MDG-based microgels at the moment. From the viewpoint of producing new materials for biomedical applications, it is of great interest to design and synthesize this three-dimensional macromolecular architecture with saccharide derivatives. Moreover, isopropylidene groups, the hydrophobic protecting groups of the sugar, could be hydrolyzed by acidolysis, increasing the hydrophilicity and giving well-defined glucose-carrying water-soluble units.

When microgel particles are based on temperature responsive polymers exhibiting a lower critical solution temperature (LCST), one of the most important characteristics is their volume phase transition at a critical temperature (VPTT). Both critical temperatures have been investigated by various experimental techniques, such as the cloud point method [17], differential scanning calorimetry [18], viscosimetry [18], fluorescence [19], infrared spectroscopy (IR), pH measurements to observe slow hydrogen–deuterium exchange [20,21], surface tension [22], nuclear magnetic resonance spectroscopy (NMR) [23], atomic force microscope (AFM) [24] and static and dynamic light scattering. Dynamic light scattering (DLS) is frequently used [25,26] to analyze the swelling behavior of microgels.

In our previous works [27,28] we presented the synthesis and characterization of PVCL-based microgels and the effect of the concentration and type of cross-linker. We also reported [29] the evidence of the hydrolysis process observed in the emulsion polymerization reactions carried out to synthesize PVCL-based microgels. When potassium persulfate (KPS) is used as initiator it is extremely important to add a buffer to the polymerization mixture in order to avoid the side reactions suffered by the monomer VCL. These side reactions should be avoided when the final material is used in biomedical applications.

In this work, the synthesis and characterization of optimized buffered polymerization reactions to produce two new families of microgels based on VCL is described. In one case, microgel particles were synthesized by using VCL as main monomer and *N*,*N*′-methylenebisacrylamide (BA) as cross-linker, whereas in the synthesis of another type of microgel particles, the sugar-based comonomer 3-MDG was incorporated to the recipe with the aim of both increasing the biocompatibility of the microgels and controlling the hydrophobic/hydrophilic balance of the particles. All polymerization reactions were initiated by potassium persulfate (KPS). Sodium dodecyl sulfate (SDS) was used as surfactant and sodium bicarbonate was the buffer. In this way, preparation of stimuli-responsive colloidal particles with defined size and enhanced monomer stability against hydrolysis was achieved. This work deals with the kinetics of the copolymerization reactions of VCL with BA, and those of VCL with BA and 3-MDG, carried out to produce the corresponding microgel particles, especially focusing our attention on the partial conversion evolutions of VCL and BA. The evolutions of the hydrodynamic average particle diameters at different temperatures were measured by means of photon correlation spectroscopy (PCS). The VPTT of the final microgel particles was determined from the average hydrodynamic diameter versus temperature curve. Transmission electron microscopy (TEM) was used for the direct observation of the new microgel particles.

2. Experimental

2.1. Materials

The monomer, *N*-vinylcaprolactam (VCL, Aldrich); the initiator, potassium persulfate ($K_2S_2O_8$, KPS, Fluka); the buffer, sodium bicarbonate ($NaHCO_3$); the cross-linker, *N*,*N*′-methylenebisacrylamide (BA, Aldrich); the surfactant, sodium dodecyl sulfate (SDS, Aldrich), and the ^1H NMR standard, sodium acetate ($NaC_2H_3O_2$) were used as supplied. The sugar-based monomer 3-MDG was synthesized in our laboratory [30]. Doubled deionized (DDI) water was used throughout the work.

2.2. Emulsion polymerization in a batch reactor

2.2.1. Synthesis of poly(VCL-co-BA) and poly(VCL-co-BA-co-3-MDG) microgels

Two families of microgel particles were synthesized in a batch reactor by emulsion copolymerization. In the synthesis of poly(VCL-*co*-BA) microgels, VCL was used as main monomer and BA as cross-linker, whereas in the synthesis of poly(VCL-*co*-BA-*co*-3-MDG) microgels, the sugar-based monomer 3-MDG was used together with VCL and BA. SDS was used as surfactant and potassium persulfate as initiator. Poly(VCL-*co*-BA) microgel particles were prepared by using 1 wt.% of VCL and different amounts of initiator (0.5, 1.0, and 1.5 wt.% with respect to VCL) at two different reaction temperatures (60 and 70 °C), cross-linker (2 and 4 wt.% with respect to VCL), and surfactant (4 and 8 wt.% with respect to VCL). All the reactions were carried out using a buffer concentration equal to that of initiator. Table 1 shows the recipes and reaction conditions used in the production of cross-linked poly(VCL-*co*-BA) microgel particles.

In the synthesis of poly(VCL-*co*-BA-*co*-3-MDG) microgels 1 wt.% of the sum (VCL + 3-MDG) but different ratios of VCL to 3-MDG (VCL/3-MDG: 100/0, 87/13, 79/21, 70/30, 63/37) were used. The polymerizations were carried out at 70 °C and the concentrations of cross-linker and surfactant were 4 wt.%, and initiator and buffer 1 wt.%; the - entire wt.% was with respect to the sum of monomers.

The polymerization reactions were carried out in a batch reactor. The batch polymerization equipment consists of a 500 mL jacketed glass reactor fitted with a reflux condenser, stainless steel stirrer, sample device, and nitrogen inlet tube. Once the main monomer, the cross-linker and the surfactant were placed into the reactor, the reactor mixture was heated at a desired temperature, stirred at

Table 1
Recipes used for the production of cross-linked poly(VCL-*co*-BA) microgel particles in a batch reactor.

Reaction	BA*	$K_2S_2O_8$*	$NaHCO_3$*	SDS*	T (°C)
1	4	0.5	0.5	4	70
2	4	1.0	1.0	4	70
3	4	1.5	1.5	4	70
4	4	0.5	0.5	4	60
5	4	1.0	1.0	4	60
6	4	1.5	1.5	4	60
7	2	0.5	0.5	4	60
8	4	0.5	0.5	8	60

Reaction conditions: rpm, 400; reaction time, 5 h; VCL, 1 wt.%.
Variables: Concentration of KPS and $NaHCO_3$, BA, SDS, and reaction temperature.
* wt.% with respect to VCL.

400 rpm, and purged with nitrogen for 1 h before starting the reaction. A shot of KPS and $NaHCO_3$ was added and the reaction mixture was stirred for 5 h under nitrogen atmosphere at a desired temperature. Once the reaction was over, the reaction mixture was cooled to 25 °C. The final dispersions were filtered through a glass wool.

2.3. Characterization of the microgel particles

During the polymerization, samples were withdrawn from the reactor at regular sampling times and adding hydroquinone as inhibitor quenched the polymerization. These samples were analyzed to determine the evolution of the partial conversions of VCL, 3-MDG, and BA.

Prior to the colloidal characterization of the microgel particles, microgels were dialyzed against distilled water to remove non-reacted reagents and impurities. Dialysis was allowed to run until the dialysate was close to that of DDI (2 μS/cm).

2.3.1. Polymeric characterization

2.3.1.1. Partial and global conversions. The evolution of the partial conversions of BA and VCL in the synthesis of poly(VCL-*co*-BA) microgels was determined by proton nuclear magnetic resonance spectroscopy (^{1}H NMR). In the synthesis of poly(VCL-*co*-BA-*co*-3-MDG) microgels, in which 3-MDG was added, only the final partial conversions of VCL, BA, and 3-MDG were analyzed by means of ^{1}H NMR. The sample preparation and the conditions used to record the NMR spectra were the same as described in our previous works [28,29]. ^{1}H NMR spectra were recorded at 500 MHz on a Bruker AVANCE spectrometer using D_2O/H_2O solution and sodium acetate as standard. In the ^{1}H NMR tube, 60 μL of deuterium oxide were added to 300 μL of microgel dispersion withdrawn from the reactor at a desired reaction time. Then, 300 μL of DDI water with the standard were added.

The partial conversions by ^{1}H NMR ($X_{i(NMR)}$) were determined as described previously [28] and the global conversions (X_G) were calculated by taking into account the partial conversions as follows:

$$X_G = \frac{(VCL_o X_{VCL}) + (BA_o X_{BA})}{(VCL_o + BA_o)} \times 100$$

where, VCL_o and BA_o are the initial VCL and BA amounts in the recipe.

2.3.1.2. Thermal behavior: glass transition temperature. In order to compare the thermal properties of the cross-linked PVCL with those of PVCL homopolymers, the glass transition temperature (T_g) of the microgel particles synthesized in reaction 2 (amount of initiator, 1 wt.% with respect to VCL, amount of cross-linker, 4 wt.% with respect to VCL, reaction temperature 70 °C, and amount of buffer, 1 wt.% with respect to VCL) was obtained by using a differential scanning calorimeter (DSC) (Perkin Elmer, Pyris 1). The measurements were carried out by adding 12 g of lyophilized microgel particles in the sample holder, at a temperature range of 50–240 °C with a heating rate of 20 °C/min.

2.3.2. Colloidal characterization

Colloidal characteristics, such as the evolution of the hydrodynamic average particle diameter during the polymerization reactions at different temperatures were measured by PCS. Samples were prepared at particle concentration of 0.05 wt.% in clean vials. The sample was placed in the cell compartment of the light scattering instrument and was equilibrated at the measurement temperature for 6 min prior to analysis. Measurements were carried out as a function of temperature from 15 to 55 °C (every 10 °C) for the particles withdrawn during the reaction and from 10 to 55 °C (every 2.5 °C) for the final microgel particles. The VPTT was determined and established as the temperature corresponding to the inflection point in the average diameter versus temperature curve.

Transmission electron microscopy (TEM) was used for the direct observation of the microgel particles. TEM (Hitachi H-7000 FA) with a cryo-holder was used to analyze the microgel particles obtained in reaction 2. The samples for TEM observation were prepared in two different ways. First, the sample was prepared by placing a drop of latex diluted to 0.1% solids content onto a formvar/carbon coated copper grid. In the second way, the sample was prepared by adding a drop of a 0.5% aqueous solution of phosphotungstic acid (PTA) negative staining into the diluted sample of 0.1% solids content. Then, a drop of dilute sample was placed on a formvar/carbon coated copper grid.

3. Results and discussion

3.1. Kinetic features

Fig. 1 shows the evolutions of the partial conversions of VCL and BA calculated for the reactions carried out with 0.5, 1.0, and 1.5 wt.% of initiator at two different temperatures (60 and 70 °C), 2 and 4 wt.% of cross-linker, and 4 and 8 wt.% of surfactant with respect to VCL. All curves show that the cross-linker BA is consumed much faster than the main monomer VCL. This fact means that BA is more reactive than VCL. In addition, BA is consumed (final partial conversion of 100%) in reactions carried out with different amounts of initiator (1.5, 1.0, and 0.5 wt.%) at 60 °C by 15, 25, and 36 min, respectively; in reactions in where different

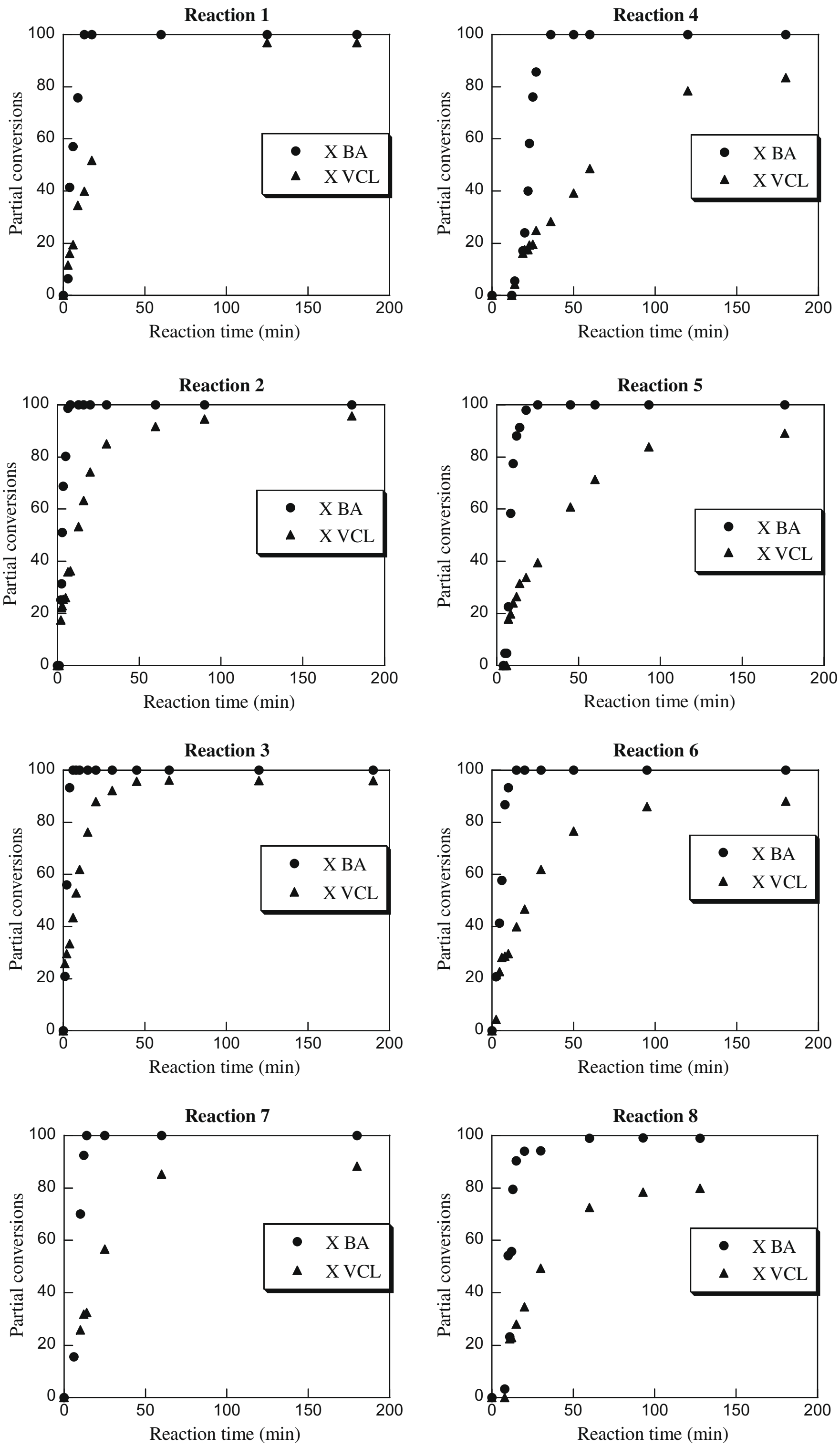

Fig. 1. Evolutions of the partial conversions of VCL and BA calculated for reactions carried out with 0.5, 1.0, and 1.5 wt.% of initiator at 70 °C (reactions 1, 2, and 3), and at 60 °C (reactions 4, 5, and 6); 2 and 4 wt.% of cross-linker (reactions 7 and 4); 4 and 8 wt.% of surfactant (reactions 4 and 8), all % with respect to VCL.

amounts of initiator (1.5, 1.0, and 0.5 wt.%) where used at 70 °C the cross-linker is consumed by 6, 8, and 13 min, respectively; in reaction carried out with 0.5 wt.% of initiator, 2 wt.% of cross-linker and at 60 °C (reaction 7) by

14 min; and in reaction carried out with 0.5 wt.% of initiator and 8 wt.% of surfactant at 60 °C (reaction 8) BA is consumed by 50 min. However, VCL took longer to achieve final conversion. Therefore, this opened the possibility of thinking that in the final microgel particles exist a zone of high cross-link density and a zone of low cross-link density. In reaction carried out by using 0.5 wt.% of initiator at 60 °C (reaction 4), the partial conversion evolution of VCL showed an inhibition period of 12 min. The presence of oxygen in the reaction medium prolongs the induction period [31]. Although the medium was purged with nitrogen for 1 h before starting the polymerization reaction and it was continuously purged with nitrogen during the reaction, the presence of dissolved oxygen acted as inhibitor delaying the starting of the reaction.

As can be seen in Fig. 1, BA achieved 100% final conversion in all reactions whereas VCL was not consumed totally. In reactions carried out at 60 °C (reactions from 4 to 8) the final partial conversion of VCL was about 85% whereas in reactions carried out at 70 °C (reactions from 1 to 3) it was about 95%. When partial conversions are observed as a function of reaction temperature at fixed initiator concentration (reactions 1 and 4; 2 and 5; 3 and 6) it can be seen that the higher the reaction temperature the faster the partial conversion evolution. Both monomers, VCL and BA, reacted faster in reactions carried out at 70 °C than in reactions carried out at 60 °C as expected, due to the higher decomposition rate of the initiator KPS when increasing reaction temperature.

By analyzing the partial conversions as a function of cross-linker concentration (reactions 4 and 7), it can be observed that the lower the cross-linker concentration, the faster the partial conversion of VCL. When 4 wt.% of BA was used, the particles were initially more cross-linked than in the case of 2 wt.%. Consequently, the growing of the particles was more difficult in the first case. Moreover, when partial conversions are observed as a function of surfactant concentration (reactions 4 and 8), it can be seen that in the reaction carried out with 4 wt.% of surfactant, the partial conversion of VCL presented a higher inhibition period and lower polymerization rate than that of the reaction carried out with 8 wt.%. In this case, the higher amount of surfactant provokes the formation of a higher number of particles, increasing in this way the polymerization rate.

Once partial conversions of VCL and BA were calculated, the evolutions of the global conversions were obtained. Fig. 2 shows the global conversions as a function of reaction time in reactions carried out with different amounts of initiator at 60 °C [Fig. 2(a)] and 70 °C [Fig. 2(b)]. As can be observed, the higher the initiator concentration (from 0.5 to 1.5 wt.%), the faster the consumption of the monomers at 60 and 70 °C. The same effect as observed in the case of the partial conversions. A higher concentration of initiator led to the formation of a higher concentration of active radicals coming from the initiator and as a result, higher polymerization rates were obtained. When the global conversions as a function of initiator at a given temperature were analyzed, the higher the initiator wt.% with respect to VCL, the faster the polymerization rate; being the final global conversions almost the same at each temperature. Moreover, final global conversions are lower when reaction temperature is the lowest, as expected.

In Fig. 3, the evolutions of the global conversions for the reactions carried out by changing the amounts of cross-linker and surfactant are shown to analyze these effects on the kinetics of the polymerization process. Fig. 3(a) shows the global conversions as a function of reaction time in the reactions carried out with 2 and 4 wt.% of cross-linker with respect to VCL at 60 °C. As can be seen, the reaction carried out with 2 wt.% of BA reacted slightly faster than that carried out using 4 wt.% of cross-linker. The evolution of the global conversion is mainly affected by the evolution of the partial conversion of VCL due to the higher amount of VCL than that of BA in the recipe. Moreover, in the determination of X_G the value of the term (BA_oX_{BA}) is very low comparing to that of (VCL_oX_{VCL}). As described earlier, when partial conversions of BA and VCL are compared (Fig. 1) in both reactions, BA reacted very fast and achieved 100% final conversion whereas the evolutions of the partial conversion of VCL in reactions carried out with 2 or 4 wt.% were different. In that carried out with 4 wt.% of cross-linker, the polymerization rate was slower than that of the reaction carried out by using 2 wt.% of cross-linker. In this way, the differences observed in global conversions come from the different partial conversion evolution of VCL in each reaction.

On the other hand, the effect of the surfactant concentration on the evolution of the global conversion at 60 °C was analyzed [Fig. 3(b)]. The differences observed came

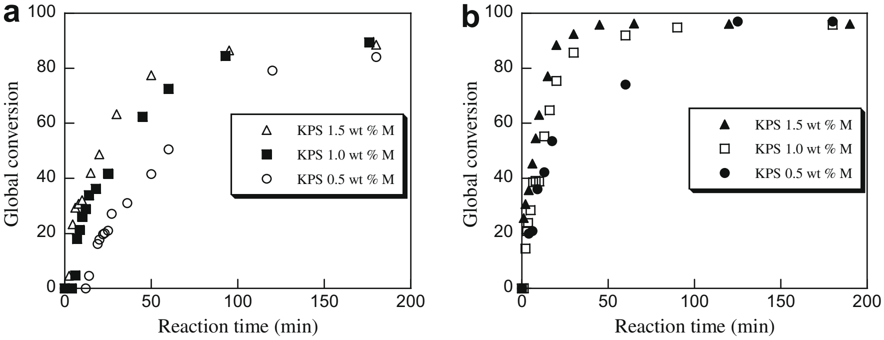

Fig. 2. Evolution of the global conversions for the reactions carried out using 0.5, 1.0, and 1.5 wt.% of initiator with respect to VCL at 60 °C (a) and 70 °C (b).

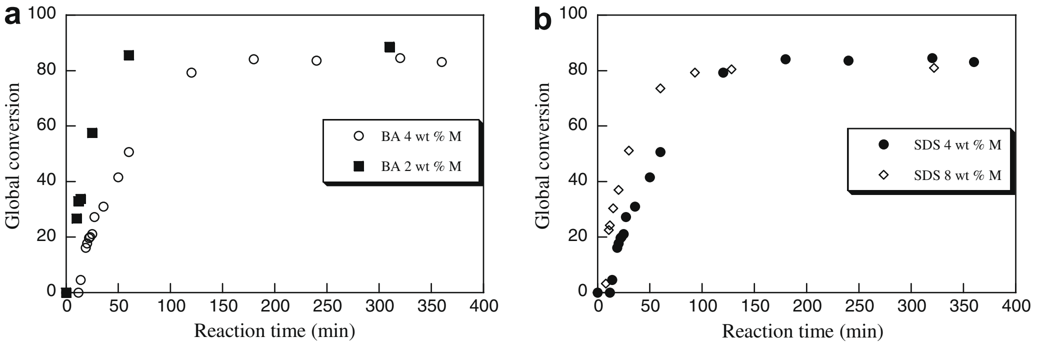

Fig. 3. Evolution of the global conversions for the reactions carried out using 2 and 4 wt.% of cross-linker (a), and 4 and 8 wt.% of surfactant (b) at 60 °C.

from the different evolutions of the partial conversion of VCL in reactions carried out with 4 and 8 wt.% of surfactant (Fig. 1), as in the previous case. The final conversion values were almost the same in both reactions.

In the family of microgels where three monomers were used (VCL as main monomer, BA as cross-linker and 3-MDG as sugar-based monomer), the final partial conversions were determined by using the ^{1}H NMR data corresponding to the last sample withdrawn from the reaction mixture. As can be seen in Table 2, BA and 3-MDG achieved a conversion of 100% in all cases. In the case of the main monomer, the results show that there is a limiting conversion. In reactions where VCL to 3-MDG ratios were 63/37, 70/30, and 79/21 the same result was obtained (83%). By decreasing the concentration of 3-MDG a higher conversion was achieved (VCL/3-MDG 87/13, 88%) and the highest conversion was obtained when 3-MDG was not added: 96%. The limiting conversion for VCL was attributed to the gel effect inside the particles due to the incorporation of the viscous and hydrophobic sugar-based monomer to the recipe together with its high partial conversion achieved.

3.2. Glass transition temperature

The influence of the cross-linker (BA) on the thermal behavior of poly(VCL-*co*-BA) lyophilized microgel particles was investigated by means of DSC. Fig. 4 shows the T_g of the microgel particles obtained in reaction 2, and the glass transition temperature was found to be 200 °C. This value is much higher than the T_g of dry and pure PVCL (145 °C) determined experimentally by Kirsch et al. [32] and Meeussen et al. [33] VCL had a cyclic structure and could be considered as a hard component. When BA was added, BA cross-linker units gave higher rigidity to the PVCL chains, and consequently, enhanced the T_g.

Table 2
Final partial conversions of VCL, BA, and 3-MDG for poly(VCL-*co*-BA-*co*-3-MDG) microgels.

VCL/3-MDG	Conversion of VCL (%)	Conversion of BA (%)	Conversion of 3-MDG (%)
100/0	96	100	–
87/13	88	100	100
79/21	83	100	100
70/30	83	100	100
63/37	83	100	100

3.3. Evolution of the hydrodynamic average particle diameters

As in the case of the conversions, different samples were withdrawn from the reactor at different reaction time with the aim of analyzing the evolution of the average hydrodynamic diameters of the microgel particles as a function of temperature by using PCS. This analysis will give information about which are the conditions required for the onset of the swelling-de-swelling behavior.

In Fig. 5, the average diameters as a function of the temperature of the medium in reactions carried out with different amount of initiator (1.5, 1.0, and 0.5 wt.%) at 60 and 70 °C, and in reactions carried out with 2 wt.% of cross-linker and 8 wt.% of surfactant are shown, respectively. It is very important to note that in all reactions and in the samples withdrawn at very low reaction times, the particles did not present swelling-de-swelling behavior. From a certain reaction time on, the particles started to be temperature-sensitive. This reaction time, referred as t_{VPTT}, is different and characteristic depending on the type of reaction. Moreover, in each reaction the corresponding partial conversions of VCL and BA at t_{VPTT} were determined (Table 3).

As can be observed in Table 3, the particles presented the swelling-de-swelling behavior when the conversion of VCL

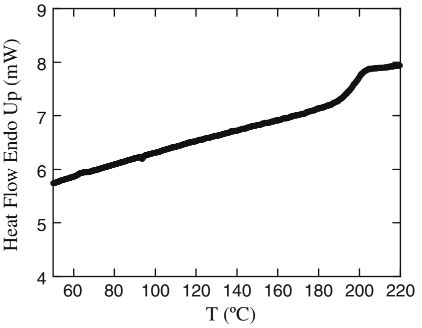

Fig. 4. DSC analysis for the dried microgel particles obtained in reaction 2.

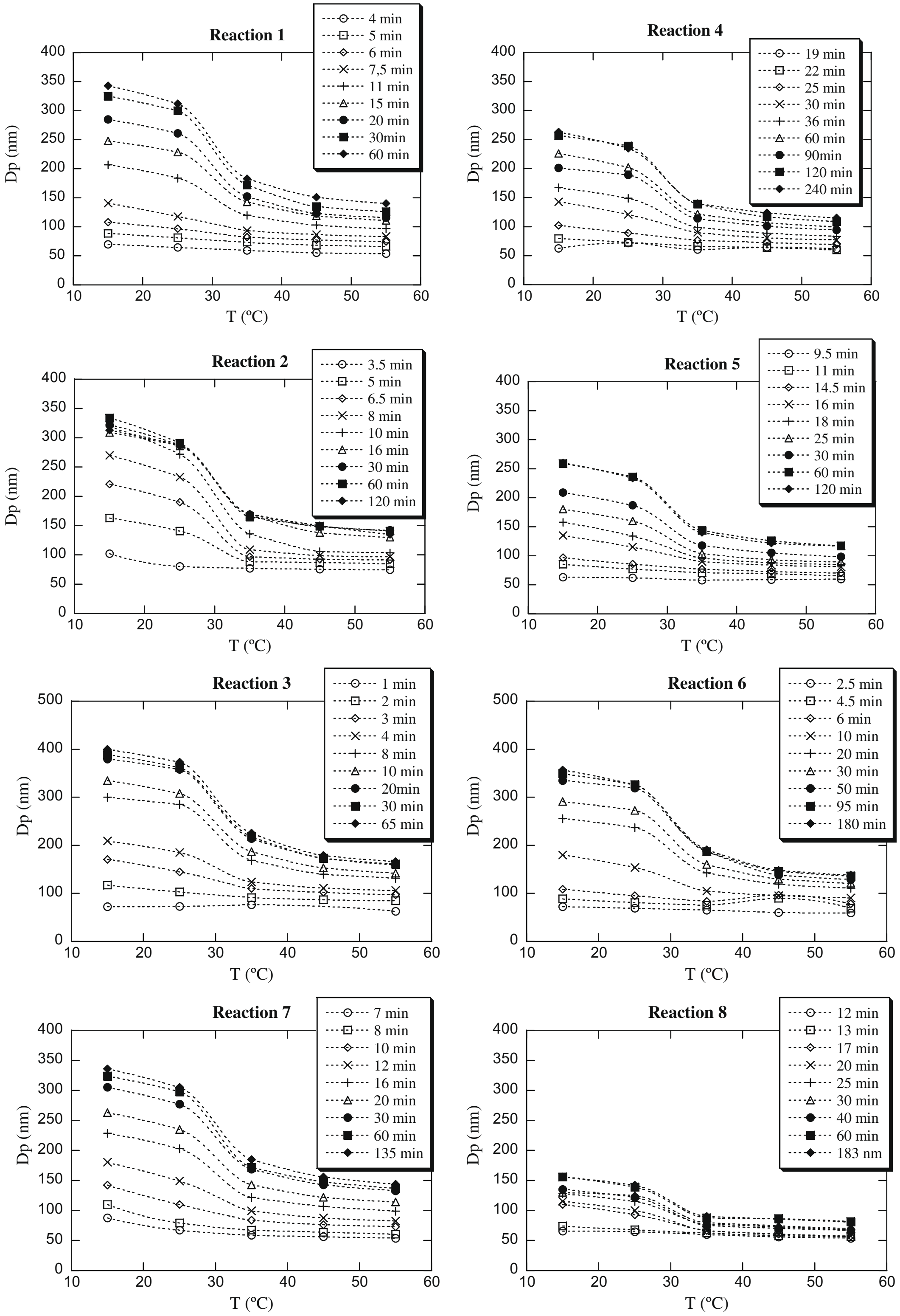

Fig. 5. Average diameters as a function of the temperature of the medium for the samples withdrawn at different reaction times in reactions carried out varying the initiator (at 70 and 60 °C) (reactions from 1 to 6), cross-linker wt.% (reactions 4 and 7), and surfactant wt.% (reactions 4 and 8).

was close to 30% (between 26% and 36% depending on the reaction). When the reaction time is below the t_{VPTT}, almost all the amount of cross-linker BA was consumed and meanwhile, a low amount of VCL units was incorporated into the microgel particles. Up to react about 30% of VCL; the microgel particles were not temperature-sensitive. However, when about 30% of VCL was incorporated into the microgel particles they became temperature-sensitive (see also Fig. 5).

Moreover, the final average hydrodynamic diameters of the microgel particles obtained by using 0.5, 1.0, and 1.5 wt.% of initiator at two different temperatures (60 and 70 °C) at collapsed state (55 °C) are shown in Table 4. Depending on the concentration of initiator in the polymerization reaction, the final microgel particles presented different diameters at collapsed state; an increase in initiator concentration results in an increase in final average diameter. This fact was not what expected, since in conventional emulsion polymerization, the higher the initiator concentration, the higher the concentration of free-radicals and the lower the final average diameter because of the higher number of particles formed. However, this was not observed when microgel particles were synthesized. This fact could not be the consequence of being the global final conversions different because, as shown before, the final conversions at 60 °C and even at 70 °C did not varied as a function of the initiator concentration. The key is the evolution of the growing particles/radicals. When a high amount of initiator was added to the reaction medium, a high concentration of free-radicals together with a high concentration of growing radicals are present in the initial stages. This enhanced the possibility, at some point, for the already formed growing radicals to react with other growing radicals instead of polymerizing with the free monomer increasing in this way the diameter of the particle. At the initial stages, the growing particles were mostly formed of BA units, having some non-reacted divinyl units. If the concentration of the growing radicals is high, radicals reacted with the BA chain instead of reacting with the free BA or/and VCL. As a result, the final average diameter was larger when higher amount of initiator was used. Moreover, it has been proved that the high charge density provoked the aggregation of particles. With the aim of proving these effects, the average hydrodynamic diameters measured at 55 °C were plotted against the global conversion for the reactions carried out with 1.5, 1.0, and 0.5 wt.% of initiator at 60 °C (Fig. 6). The hydrodynamic diameters of the particles synthesized with 0.5 wt.% of initiator increase in a constant way by increasing the conversion whereas with 1.0 and 1.5 wt.% there is an increase/step in the average hydrodynamic diameter. This suggested that at this point the excess of charge (high concentrations of initiator) provoked the aggregation of the particles, giving as a result larger final diameters.

Table 3
t_{VPTTs} and the corresponding partial conversions of VCL and BA, and VPTTs for poly(VCL-*co*-BA) microgels.

Reaction	t_{VPTT} (min)	Conversion of VCL (%)	Conversion of BA (%)	VPTT (°C)
1	7.5	26	62	36.5
2	6.5	36	98	35.2
3	2	30	56	36.4
4	30	28	100	36.6
5	16	32	94	35.6
6	10	30	93	35.5
7	7	26	70	34.5
8	17	28	90	36.6

Table 4
Final average diameters at collapsed state for the reactions carried out with 1.5, 1.0, and 0.5 wt.% of initiator at 60 and 70 °C.

Reaction	KPS (wt.% M)	T_{reaction} (°C)	$\mathrm{Dp}_{55^\circ\mathrm{C}}$ (nm)
1	0.5	70	141
2	1.0	70	150
3	1.5	70	171
4	0.5	60	127
5	1.0	60	129
6	1.5	60	146

Regarding the family of poly(VCL-*co*-BA-*co*-3-MDG) microgels, Fig. 7 shows the average diameters as a function of the temperature of the medium for the samples withdrawn at different reaction times. As can be seen, at the very beginning of the reaction the microgel particles were not temperature-sensitive and the average hydrodynamic diameters not varied as a function of temperature. This fact was analyzed together with the values of the t_{VPTT} shown in Table 5. From 6.5, 80, 85, 30, and 45 min reaction time on, the particles were temperature-sensitive. In this way, when the reaction time was higher than t_{VPTT}, the microgel particles presented the swelling-de-swelling behavior; by increasing the temperature of the medium, decreased the hydrodynamic diameters. These results show that the addition of 3-MDG into the recipe provokes a delay in the onset of the swelling-de-swelling behavior comparing to that observed in reactions carried out without the sugar-based comonomer (see Tables 3 and 5).

3.4. Temperature sensitivity of final microgels and VPTT

The effect of the temperature of the medium on the final average diameters when changing the initiator concentration, reaction temperature, cross-linker and surfactant concentration was analyzed by PCS. The results show that all final microgel particles synthesized swell by decreasing temperature and shrunk at temperatures above the transition temperature (VPTT), as expected.

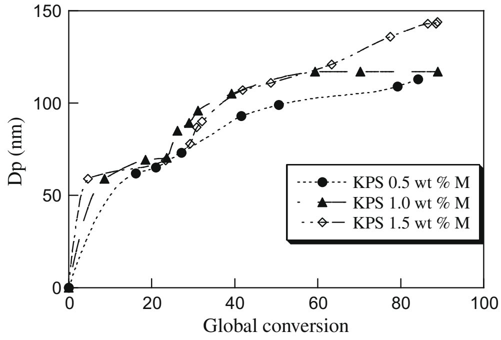

Fig. 6. Average hydrodynamic diameters of the microgel particles synthesized in reactions carried out with 1.5, 1.0, and 0.5 wt.% of initiator at 60 °C as a function of global conversion, measured at 55 °C.

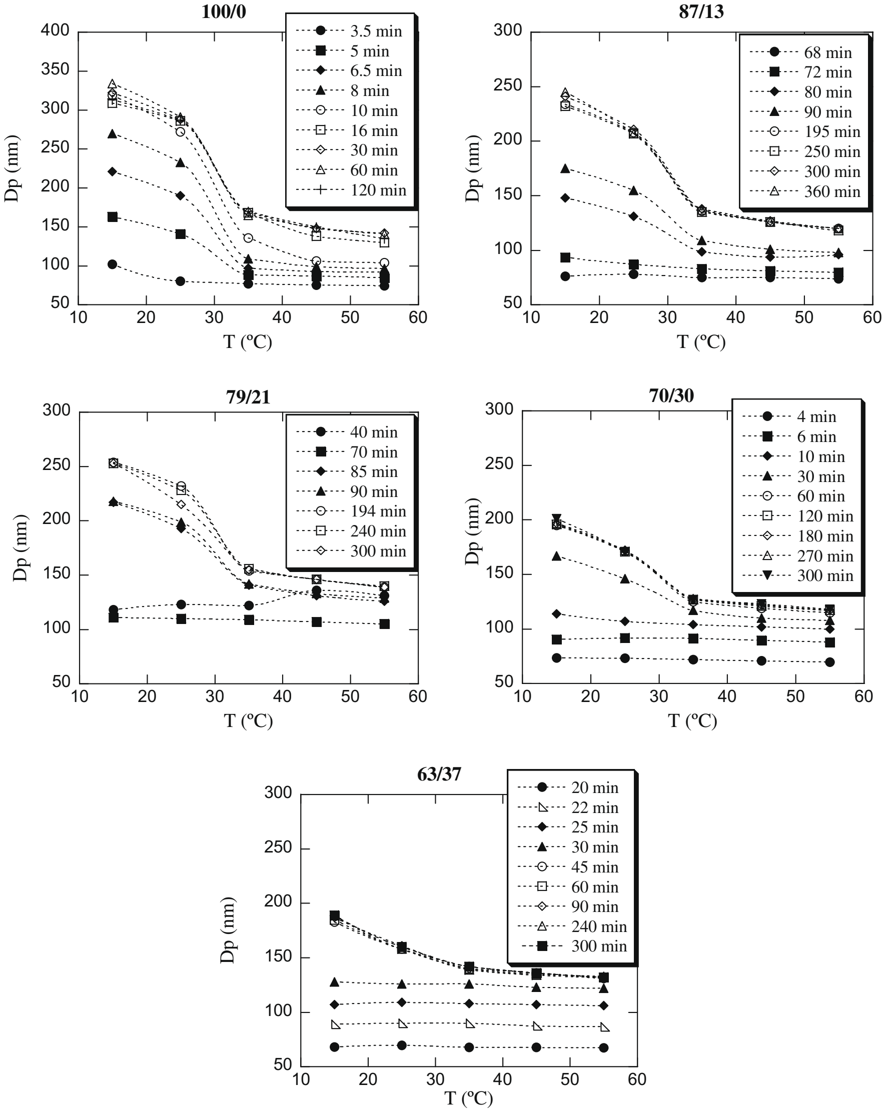

Fig. 7. Average diameters as a function of the temperature of the medium for the samples withdrawn at different reaction times in reactions carried out with different VCL/3-MDG ratios.

Table 5
t_{VPTTs} and VPTTs for poly(VCL-*co*-BA-*co*-3-MDG) microgels.

VCL/3-MDG	t_{VPTT} (min)	VPTT (°C)
100/0	6.5	35.2
87/13	80	34.7
79/21	85	34.1
70/30	30	31.4
63/37	45	29.9

Fig. 8 shows the average hydrodynamic diameters of the final microgel particles as a function of the temperature of the medium in reactions carried out with 1.5, 1.0, and 0.5 wt.% of initiator at 60 °C (a) and 70 °C (b). VPTTs values for the microgel particles were calculated from these (average diameter versus temperature) curves and determined as the temperature corresponding to the inflection point. They are also shown in Table 3. As can be seen, this value does not depend on initiator concentration and at 60 and 70 °C the VPTTs are between 35.2 and 36.2 °C. This indicates that the microstructure of the microgel particles, consisting of a high cross-linking density zone in the core and a low cross-linking density zone in the shell, together with the hydrophobic/hydrophilic balance did not vary from one reaction to another. Moreover, in all cases, the final average hydrodynamic diameter increases when the reaction temperature is increased. As shown before, when reaction temperature was 60 °C, lower final global conversions were obtained, thus smaller final average hydrodynamic diameters were achieved.

The effect of the cross-linker concentration on the temperature sensitivity of the final microgel particles is shown in Fig. 9(a). As can be seen, the microgel synthesized using 2 wt.% of cross-linker swell slightly less at low temperatures

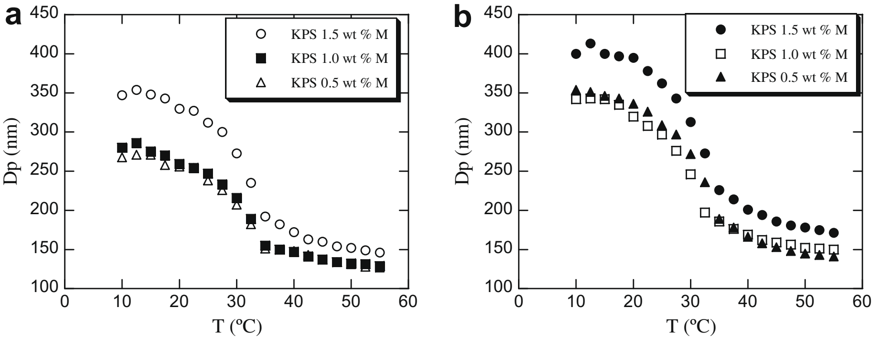

Fig. 8. Final microgel particles diameters as a function of the temperature of the medium in reactions carried out with 1.5, 1.0, and 0.5 wt.% of initiator at 60 °C (a) and 70 °C (b).

than that synthesized with 4 wt.%. At high temperatures there were no significant differences in de-swelling. It seems that in order to see the expected effect of the cross-linker on the swelling extent (the higher the cross-linker amount the lower the swelling extent) higher differences in cross-linker concentrations should be required. However, the VPTT increases by increasing the cross-linker concentration (Table 3). This increase indicates that the interaction between the polymer chains and the water molecules varies and this change is related to the increasing solubility of the cross-linker moieties at higher temperatures.

In Fig. 9(b), the final microgel particle diameters as a function of the temperature of the medium in reactions carried out varying the surfactant concentration with respect to VCL are shown. The final microgel particle at collapsed state (55 °C) was much smaller for the reaction carried using the 8 wt.% of surfactant. This fact is also observed in a conventional emulsion polymerization due to the ability of the surfactant to stabilize the small particles avoiding the aggregation between the growing ones. Having lower amount of VCL polymerized in each microgel particle, the swelling is lower than that of the particles obtained in reaction 4 when decreasing the temperature of the medium.

In addition, Table 3 shows that the use of different amounts of SDS does not change the value of the VPTT significantly. In these reactions most of surfactant is used to stabilize the microgel particles and therefore it is located on the surface of the particles. In this way, there is not surfactant in the inner part of the particles and therefore, the phase transition temperature was not affected.

In the case of the microgels synthesized using different ratios of VCL to 3-MDG, the ratio of the diameter of the swollen particles to the diameter of the collapsed particles (Dp/Dp*) as a function of temperature was analyzed (Fig. 10). The results show that the higher the amount of 3-MDG used in the recipe, the lower the swelling extent. Moreover, an increase in concentration of the sugar-based monomer results in a broadening of the temperature range over which de-swelling occurs. 3-MDG is a hydrophobic monomer and the corresponding polymer [poly(3-MDG)] is not temperature-sensitive. Therefore, by copolymerizing with VCL, the sugar-based monomer confers hydrophobicity to the particles, decreasing the swelling extent. In addition, the incorporation of 3-MDG modified the VPTT of the final microgel particles. As can be seen in Table 5, by changing the ratio of VCL to sugar-based monomer from 100/0 to 63/37, the VPTT value decreased from 35.2 to 29.9 °C. The particles obtained in reaction carried out using 37% of 3-MDG were the most hydrophobic and collapsed at the lowest temperature.

3.5. Direct observation of the microgel particles

Microgel particles synthesized in reaction 2 were analyzed by transmission electron microscopy (TEM).

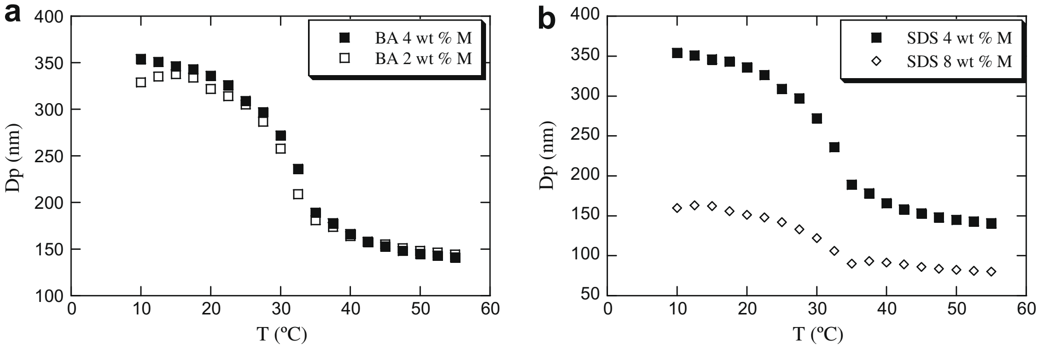

Fig. 9. Final microgel particles diameters as a function of the temperature of the medium in reactions carried out varying the cross-linker concentration (4 and 2 wt.%) (a), and in reactions carried out varying the surfactant concentration (4 and 8 wt.%) (b).

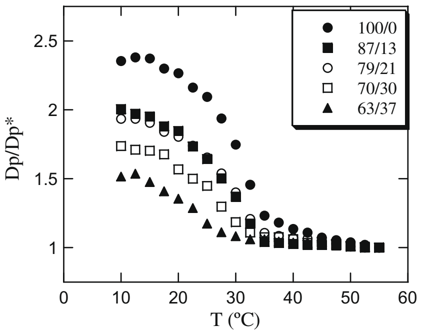

Fig. 10. Dp/Dp* as a function of the temperature of the medium in reactions carried out varying the VCL to 3-MDG ratio. Dp* is the average diameter at the shrunken state.

TEM microphotographs were obtained by using a cryo-holder. Microgel particles not stained (upper level) and stained (lower level) with phosphotungstic acid (PTA) [34] are shown in Fig. 11. The microgel particles without PTA presented different forms and sizes. Most of them were not spherical having in general diameters larger than 150 nm. As explained before, samples were prepared by adding a drop of the microgel dispersion into a cryo-holder and observed at frozen state. Being very low the temperature, the particles were frozen in the swollen state. Moreover, the microphotograph shows microgel particles in white, black, and white-black. The black aspect was due to the presence of the crystallized water in the particles whereas the white aspect was due to the non-crystallized water into the microgel particles.

The TEM microphotographs presented in the lower level indicate that there are indeed some changes by adding PTA into the microgels. The particles were dark and this suggested that the PTA is not only placed around the surface of the particles, but also went into the inner part of the microgel particles, staining in this way the inner and outer parts. In this case, the microgel particles had diameters around or smaller than 100 nm due to their dry state while observing by TEM.

4. Conclusions

Two new families of microgels were synthesized by emulsion polymerization in a batch reactor using a buffer to avoid the hydrolysis of *N*-vinylcaprolactam (VCL). On the one hand, VCL was copolymerized with *N*,*N*′-methylene-bisacrylamide (BA) to obtain temperature-sensitive microgel particles. The main interest was devoted to study the effect of the initiator, surfactant, and cross-linker concentrations, and reaction temperature on kinetic features (conversion evolution) and colloidal properties (particle size as a function of the temperature of the medium). On the other hand, VCL was copolymerized with BA and a sugar-based monomer (3-MDG). In this case, microgels with tunable swelling degree were prepared and characterized.

By analyzing the evolutions of the partial conversions, it has been shown that in all cases, BA reacted much faster than VCL and that the initiator concentration and reaction temperature have an important effect on the polymerization kinetics and final conversions. When a higher amount of initiator was used, the polymerization rate was increased. Moreover, the higher the reaction temperature the higher the final conversion. In the case of poly(VCL-*co*-BA-*co*-3-MDG) microgels, final partial conversions were determined. BA and 3-MDG achieved a complete conversion whereas VCL was not consumed totally.

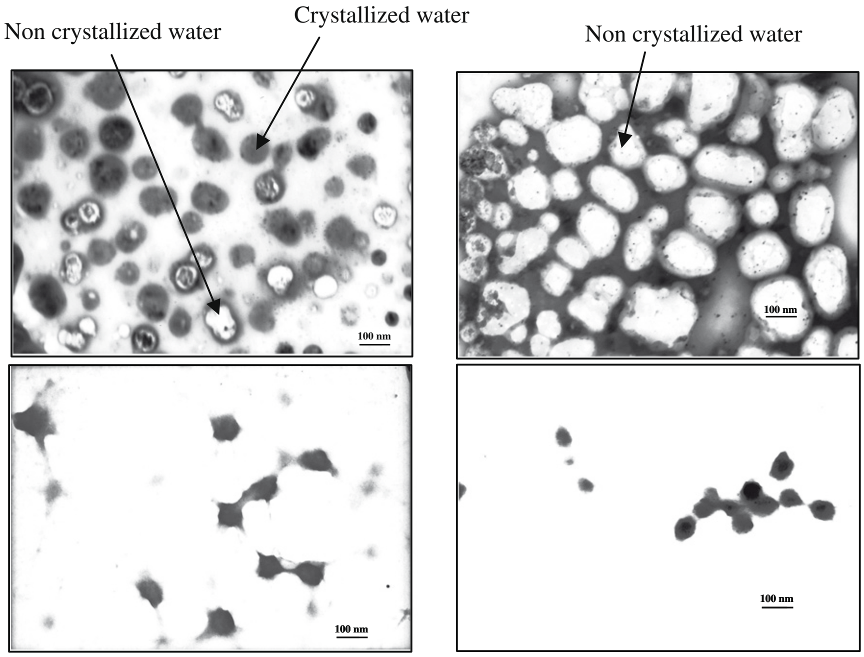

Fig. 11. TEM microphotographs of the final particles obtained in reaction 2, not stained (higher level) and stained (lower level) with PTA.

DSC determined the glass transition temperature of the polymer that constitutes the microgel particles obtained in reaction 2. By using a cross-linker (BA) as comonomer, the T_g of the homopolymer (PVCL) was enhanced from 145 to 200 °C.

With respect to the swelling-de-swelling behavior, all final microgel particles upon heating decreased their hydrodynamic diameters. However, the initially formed microgel particles were not temperature-sensitive. This was attributed to the low presence of VCL units in the copolymer forming the microgel particles, since BA reacted much faster than VCL. Initial particles were mainly formed by a high amount of BA and a low amount of VCL. Up to about 30% of VCL conversion the onset of the swelling-de-swelling behavior of microgel particles was not observed.

The VPTT was analyzed as a function of the initiator concentration, reaction temperature, surfactant and cross-linker concentrations, and ratio of VCL to 3-MDG. It was concluded that the VPTT temperature does not depend on initiator and surfactant concentrations, whereas does depend on the cross-linker concentration and ratio of VCL to 3-MDG.

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