

Incorporation of High Oil Content in Polyvinyl Acetate Nanoparticles Produced by Batch Miniemulsion Polymerization Stabilized with a Polymeric Stabilizer

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ABSTRACT: Nanoparticles (NPs) have been widely applied in the biomedical area. In order to satisfy the requirements for biomedical applications, sodium lauryl sulfate (SLS) and hexadecane, widely used as anionic surfactant and co-stabilizer, were successfully replaced by biocompatible compounds, in order to obtain poly(vinyl acetate) (PVAc) NPs via miniemulsion polymerization. The incorporation of high oil content in PVAc NPs was investigated, using different poly(vinyl alcohol) (PVOH) concentrations as polymeric surfactant. Besides the polymeric surfactant, lecithin and Miglyol 812, a triacylglycerol of saturated fatty acids obtained from coconut oil, were used as surfactant and co-stabilizer, respectively. A high Miglyol 812 content was incorporated in the PVAc NPs and the morphology was investigated by TEM. The influence of PVOH concentration on the droplet nucleation mechanism and final morphology of PVAc NPs was evaluated. High PVOH concentration favored micellar particle nucleation. According to the TEM images, hemispheres nanoparticles were obtained. © 2014 Wiley Periodicals, Inc. *J. Appl. Polym. Sci.* **2015**, *132*, 41365.

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INTRODUCTION

Miniemulsion polymerization is getting more and more attention due to the interesting feature of droplet nucleation that may provide colloidal systems with unique properties.^{1–3} For instance, miniemulsion polymerization allows the incorporation of hydrophobic active substances in a single reaction step, being a versatile and efficient technique that results in nanoparticles with typical sizes ranging from 50 to 500 nm.^{2,4} In these systems, the degradation of small droplets by monomer diffusion is minimized by the presence of a co-stabilizer and droplets are protected against coalescence by the addition of an effective surfactant.

Since the co-stabilizer remains in the nanoparticles, by choosing a specific co-stabilizer type may influence the application of the final colloidal system. Indeed, the majority of the formulations described in literature are based on hexadecane as co-stabilizer, restricting its biomedical application.⁵ Therefore, biocompatible components such as Miglyol 812, Neobee M-5, açai, jojoba and andiroba oils have been used in order to replace hexadecane.^{6–11} The encapsulation of a high Miglyol 812 content in PVAc nanocapsules by miniemulsion polymerization was reported by Rajot et al., however, microscopy images or other analyses that could confirm its morphology were not shown.⁷ Regarding the effect of co-stabilizer, it was previously observed the decrease of the reac-

tion rate and average molar mass when hexadecane (alkane hydrocarbon) is replaced by Miglyol 812 (triacylglycerol of saturated fatty acid) in VAc miniemulsion polymerization.^{6,8} This fact was attributed to chain transfer reactions to Miglyol 812 during VAc polymerization, and this effect became even more pronounced when Miglyol 812 was replaced by Castor oil (triacylglycerol of unsaturated fatty acid). In addition, the surfactants used for preparation of nanoparticles also have a strong influence not only on the colloidal properties, but also on the application properties of these colloidal systems.¹² Thus, the use of poly(vinyl alcohol) (PVOH) as polymeric stabilizer, combined with a low molar mass surfactant for vinyl acetate (VAc) polymerization, imparts to colloidal systems better emulsion fluidity, higher shear resistance, superior wet primary tackiness and chemical stability, that are useful in the manufacture of latex paints, paper coatings and adhesives.^{13–15} Additionally, due to its biocompatibility, non-toxicity, good hydrophilicity and semi-permeability, PVOH hydrogel has been widely used for scaffolds, embolic materials, contact lenses and wound dressings in biomedical applications.¹⁶

Usually, in emulsion and miniemulsion polymerization processes, a partially hydrolyzed PVOH with 88% hydrolysis degree is used as polymeric stabilizer in order to exploit its hydrophobic-hydrophilic characteristics.^{1,12–15,17} Kim et al. investigated the use of 88% hydrolyzed PVOH as stabilizer in

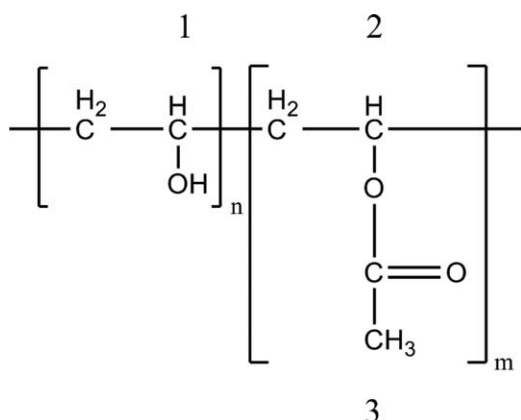


Figure 1. Molecular structure of partially hydrolyzed poly(vinyl alcohol) (PVOH).

acrylic miniemulsion polymerization.¹⁸ It was observed that the droplet size decreased exponentially with PVOH concentration and then leveled off. The stability in VAc polymerization is provided by both, adsorbed and grafted PVOH.^{13,14} PVOH adsorbs on the particle surface with the hydrophobic acetate units providing the primary anchoring segments, and the hydrophilic vinyl alcohol blocks project out into the aqueous phase as stabilizing moieties.^{12,14} As expected, Kim et al. observed that the number of adsorbed PVOH chains on the droplets increased and then was almost independent of the PVOH concentration, showing surface saturation.¹⁸ Bohórquez et al. proposed an optimal 88% hydrolyzed PVOH concentration as 2 to 4 wt % to maximize droplet nucleation in high solids content miniemulsion polymerization of VAc and VeoVa10.¹ The results obtained showed that higher PVOH concentrations lead to particle formation by a similar micellar nucleation mechanism, due to the increase of free PVOH in the aqueous phase, which might form aggregates with the same characteristics of micelles. But most of VAc polymerization PVOH stabilized studies concerned about the improvement of the degree of grafted PVOH.^{1,12–15,17–20} Grafting of vinyl acetate onto PVOH can occur by hydrogen abstraction from either of the two backbone tertiary C-H bonds, numbered 1 and 2 and from the methyl side groups of the partially hydrolyzed chain of the PVOH, 3, Figure 1, followed by propagation with monomer.¹⁹ It was reported that excessive grafting may lead to a less efficient, too hydrophobic stabilizer.¹ Combinations of fractionation and selective solubilization techniques were previously used to measure the

degree of grafting, and consequently, the free PVOH and adsorbed PVOH fractions.^{19,20} The studies discussed above involved the determination of the grafting degree during mostly miniemulsion polymerization of VAc using 88% hydrolyzed PVOH and 0 to 4 wt % of co-stabilizer related to monomer.^{1,12–15,17–20} Recently, Peruzzo et al. reported the preparation by miniemulsion polymerization of PVOH stabilized polyvinyl acetate (PVAc) nanoparticles loaded with clay and TEM images showed clearly the presence of solid material inside the nanoparticles.²¹

The current work studies the miniemulsion polymerization of VAc aiming the incorporation of high oil content, using biocompatible and biodegradable compounds, such as, Miglyol 812 as co-stabilizer and PVOH (with different hydrolysis degrees and molar masses) and lecithin as surfactants. The chosen surfactant and co-stabilizer for the nanoparticle preparation satisfy the requirements for biomedical applications as delivery systems of hydrophobic drugs. Drug loading efficiency, as well as release kinetics depend on the polymer-drug interactions, continuous phase properties and NPs morphology and may be impacted by the incorporation of high amounts of an oil as Miglyol 812. The morphology investigated by transmission electron microscopy (TEM) images revealed the achievement of hemispheres nanoparticles and the use of a polymeric stabilizer (PVOH) allowed minimizing the increase of the PVAc nanoparticle size during polymerization (observed during polymerizations without PVOH, but not for the unpolymerized miniemulsion kept under the same conditions).

EXPERIMENTAL

Materials

Vinyl acetate (VAc) was used as monomer in the miniemulsion polymerizations. Lecithin from Alfa Aesar was used as surfactant. In addition, three different commercial polyvinyl alcohol (PVOH) types were used as polymeric stabilizer (all were purchased from Polysciences Inc. with the following degrees of hydrolysis and molar masses: 98% and 25,000 g mol⁻¹, 88% and 78,000 g mol⁻¹, and 80% and 6000 g mol⁻¹). Miglyol 812 (Sasol), a triacylglycerol of saturated fatty acids, predominantly caprylic acid (50 to 65%) and capric acid (30 to 45%) obtained from coconut oil, was used as co-stabilizer and 2,2'-azo-bis-isobutironitrile (AIBN) from Vetec Química was used as initiator. Distilled water composed the aqueous continuous phase. To stop the reactions, hydroquinone aqueous solution (1 wt %) (Nuclear) was used. Figure 2 shows the chemical structures of the surfactant and co-stabilizer used in this work.

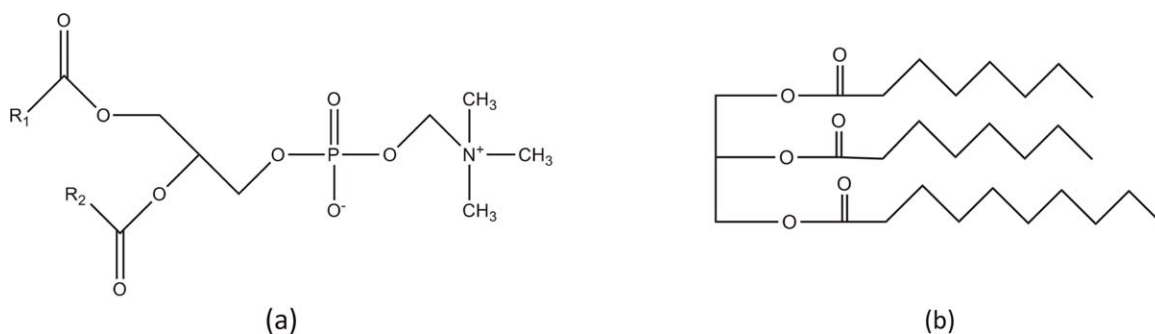


Figure 2. Molecular structure of a) lecithin, where R1 and R2 are typically linear aliphatic chains with 15 or 17 carbon atoms and up to four cis double bonds and b) Miglyol 812.

Table I. Formulations of VAc Miniemulsion Polymerizations with AIBN as Initiator

Reactants	Amount (wt %)	Reactions	Additional Stabilizer	PVOH Amount (%) ^a
VAc	9.9			
Lecithin	0.30	P0	^b	0
Miglyol 812	9.9	P1-P4	PVOH 98% hydrolysis degree	5.0-40.0
Water	79	P5-P8	PVOH 80% hydrolysis degree	2.5-15.0
AIBN	1.15	P9-P12	PVOH 88% hydrolysis degree	15.0-30.0
Stabilizer	Variable			

^a wt % related to monomer.

^b Reaction carried out with only lecithin as surfactant.

Procedures

A blank reaction (P0) was conducted with lecithin as the sole surfactant following the formulation shown in the two left columns of Table I. All other reactions were conducted with lecithin and PVOH, as summarized in Table I.

The aqueous phase was prepared by dissolving the PVOH at 80°C for 8 h, except for 98% hydrolyzed PVOH, for which the time required was 24 h, in distilled water and then the solution was filtered. The solids content of the PVOH solution was checked gravimetrically and adjusted to the concentration of the formulation, according to Table I. The co-stabilizer (Miglyol 812), lecithin and the oil-soluble initiator were dissolved in the monomer for 50 min in a jacketed reactor at 10°C. In sequence, the organic phase and the aqueous phases were mixed together with a magnetic stirrer for 20 min in a jacketed reactor at 10°C and an ultrasound probe (Fisher Scientific, Sonic Dismembrator Model 500) was used during 4 min at 60% of amplitude to prepare the miniemulsions. Only when PVOH with 88% hydrolysis degree and 78,000 g mol⁻¹ was used, the sonication time was increased to 8 min. In order to avoid temperature increase during sonication step, which could lead to the decomposition of the organo-soluble initiator and, consequently, start prematurely the reaction, a jacketed reactor with cooling fluid at 10°C was used.

Batch polymerization reactions were carried out at constant temperature (70°C) in ampoules with diameters equal to 10 mm. Samples were removed periodically and reaction was shortly stopped with the addition of a 1 wt % hydroquinone aqueous solution. Conversion was calculated based on gravimetric data, after drying samples at 60°C in a convection oven until constant weight was obtained.

Intensity average diameters of monomer droplets (D_m) and of polymer particles (D_p) were measured by dynamic light scattering (DLS; Malvern Instruments, Nano Sizer Nano S). For these measurements, the samples were diluted in distilled water saturated with the monomer. Particle (N_p) and droplet (N_m) numbers were calculated based on intensity average particle diameter and conversion measurements.

The viscosities of the aqueous phase containing different PVOH concentrations were determined with a capillary Ubbelohde type viscometer and the procedure was checked by measuring the viscosity of pure water. A thermostatically controlled and well-stirred water bath at 70°C was used for all viscosity meas-

urements. The flow-time measurements were made using a stopwatch with a precision of ± 0.01 s. The average of three sets of flow times was used for the calculation of the viscosity of each fluid.

The final morphology of PVAc nanoparticles was studied by transmission electron microscopy (TEM) performed on a JEOL JEM 1011 microscope at an accelerating voltage of 80 kV. Due to their low glass transition temperature, PVAc particles may deform during sample drying and/or under the electron beam of the microscope. In this way, PVAc particles were negatively stained with uranyl acetate (UAc), as described by Ferguson et al., to improve the observation of particle contour.²² Generally, 1 mL of sample was diluted into 20 mL of 0.1 wt % UAc aqueous solution previously prepared. After 30 min protected against light, 5 μ L of the diluted sample were placed on a 300 mesh parlodium or, when mentioned, carbon coated copper grid and dried in the dark at room temperature. To assure representative images of the sample, several different regions of the TEM grids were analyzed.

RESULTS AND DISCUSSION

Sodium lauryl sulfate (SLS) and hexadecane, widely used as anionic surfactant and co-stabilizer, were successfully replaced by lecithin and Miglyol 812, respectively, in order to obtain biocompatible PVAc nanoparticles (NPs) via miniemulsion polymerization [Figure 3(a)].

According to the evolution of average particle sizes during the polymerization reaction [Figure 3(b)], coalescence was an important degradation process of droplets/particles until conversion achieved around 70% after 90 min of polymerization. Nanoparticles were stabilized exclusively with lecithin and Miglyol 812 (P0). The same type of behavior, increase of average particle size during polymerization, was also observed in VAc miniemulsion polymerizations with lower amounts of Miglyol 812, but did not occur in methyl methacrylate miniemulsion polymerizations with the same surfactant and co-stabilizer types and amounts.⁸ In order to verify if the increase of the particle size during VAc miniemulsion polymerizations is due to the lack of stability of the original miniemulsion, average droplet diameters of the miniemulsions kept at 70°C (without initiator and, thus, without polymerization) were measured during the same time. Obtained results [Figure 3(b)] indicate that the average droplet diameters of VAc miniemulsions prepared

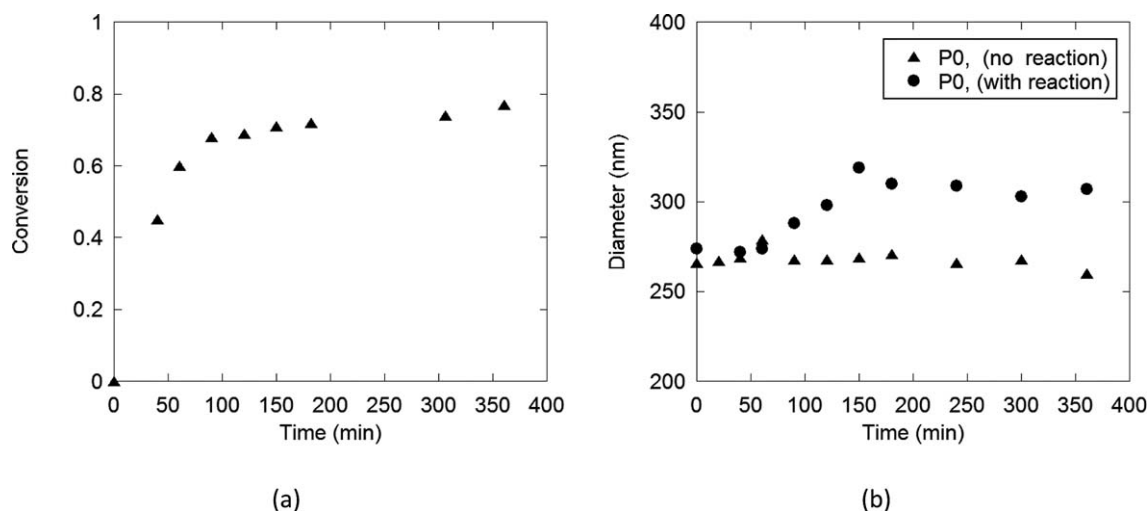


Figure 3. VAc miniemulsion polymerizations P0 using AIBN at 70°C. (a) Conversion. (b) Comparison between average droplet and particle diameters during reaction and without polymerization.

with lecithin as surfactant did not vary during 6 h of analysis. Thus, the gradual increase of the particle size throughout the VAc polymerizations is a characteristic of the polymerization of VAc. PVAc has a relatively low glass transition temperature that might favor the coalescence process. Therefore, PVOH is added as polymeric stabilizer to increase the stability during polymerization due to its grafting ability.¹² In this way, polymerization reaction without PVOH (P0) was used as reference to evaluate the effect of PVOH concentration and type on the VAc miniemulsion polymerization kinetics, average droplet and particle sizes and final nanoparticle morphology.

Effect of PVOH Concentration

Table II summarizes the effect of the PVOH type (degree of hydrolysis and molar mass) and concentration on final conversion, average initial monomer droplets and final polymer particles diameters and on the particle (N_p) and droplet number (N_m) ratio. Firstly, a comparison of polymerization kinetics with different concentrations of 98% hydrolyzed PVOH is shown in Figure 4(a). Reactions with up to 10.0 wt % of PVOH in relation to VAc showed comparable kinetics until around 180 min, despite the bigger droplet and particle sizes of reaction P2, Figure 4(b). After 180 min, particle size of reaction P2 increased

Table II. Characteristics of VAc Miniemulsion Polymerizations Initiated with AIBN

Reactions	PVOH (wt %) ^a	PVOH $\times 10^{-2}$ (mol %) ^a	D_m (nm)	D_p^b (nm)	N_p^b/N_m	X_f (%)
P0	0.0	0.0	274	311	0.62	81
PVOH 98% hydrolyzed and molar mass 25,000 g mol ⁻¹						
P1	5.0	1.72	286	325	0.63	71
P2	10.0	3.44	298	450	0.28	57
P3	20.0	7.88	404			
P4	40.0	15.76	502			
PVOH 80% hydrolyzed and molar mass 6000 g mol ⁻¹						
P5	2.5	3.59	377	363	1.02	88
P6	5.0	7.17	296	300	0.90	72
P7	10.0	14.3	245	246	0.91	80
P8	15.0	21.5	211	238	0.64	82
PVOH 88% hydrolyzed and molar mass 78,000 g mol ⁻¹						
P9	15.0	1.82	306	315	0.83	90
P10 ^c	15.0	1.82	292	294	0.89	85
P11 ^c	25.0	2.99	266	315	0.54	93
P12 ^c	30.0	3.64	266	292	0.68	95

^aRelated to monomer.

^bAt the final conversion (X_f).

^cSonication for 8 min, instead of 4 min as in all other reactions.

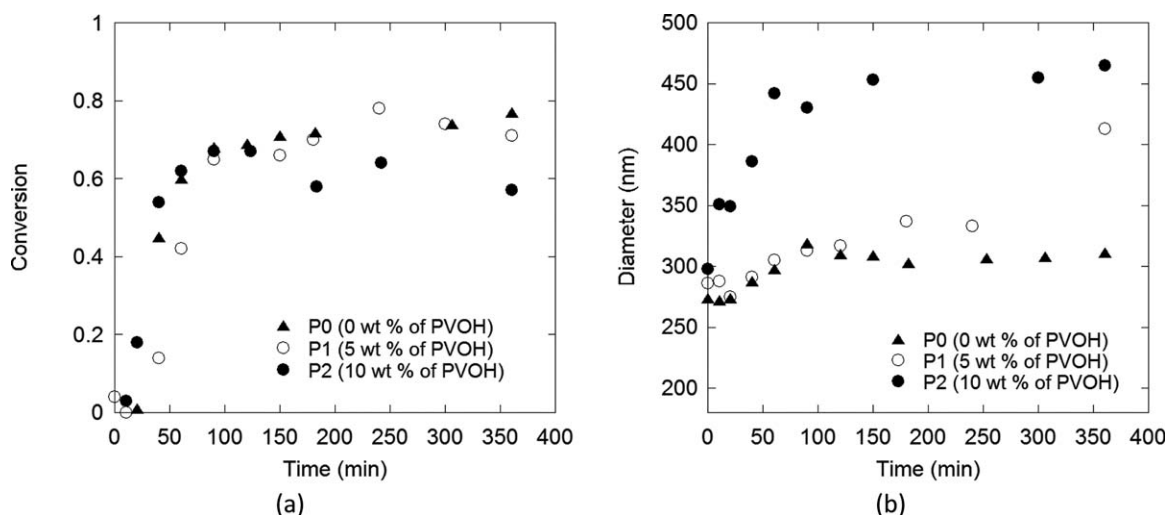


Figure 4. Evolution of properties during VAc miniemulsion polymerizations using 98% hydrolyzed PVOH and $M_w = 25,000 \text{ g mol}^{-1}$ as polymeric stabilizer. (a) Conversion. (b) Average droplet and nanoparticle diameters (nm).

severely, indicating a reduced stability and the formation of larger aggregates hampered representative sampling and thus led to artificially low conversions of P2.

TEM images evidenced the broad size distribution of particles P2 (Figure 5). For this analysis, the nanoparticles were treated with uranyl acetate. Uranyl acetate (UAc) is able to stain hydroxyl groups present in the molecular structure of partially hydrolyzed PVOH, evidencing the PVOH location on the particle surface.

Due to the high Miglyol 812 content, phase separation occurred inside PVAc nanoparticles (P2) stabilized with 10 wt % PVOH (98% hydrolyzed) and, according to TEM images shown in Figure 5, those present hemisphere morphology. Three different materials were found by TEM images (Figure 5). The darkest material is stained PVOH forming a structure around the PVAc (gray material) particle, which is partially engulfing Miglyol 812, the brightest material. Due to the fact that the nanoparticles were not cleaned from the free PVOH in the continuous

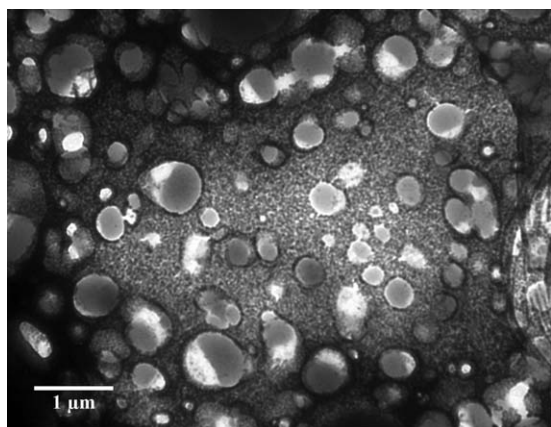


Figure 5. TEM images of final sample P2 stabilized with 10 wt % related to monomer of PVOH 98% hydrolyzed and $25,000 \text{ g mol}^{-1}$ (negatively stained with uranyl acetate).

phase, a negative contrast can be observed in the TEM image. PVAc/Miglyol 812 hemisphere nanocapsules without PVOH were already previously shown.⁸ The presence of nanoparticles with different ratio between PVAc and Miglyol 812 might be attributed to degradation processes. Diffusional degradation may increase the Miglyol 812 concentration in the smaller particles. Additionally, coalescence might contribute with a random effect on PVAc/Miglyol 812 ratio inside the final NPs since if several small NPs with high amount of Miglyol 812 coalesce big NPs with a high amount of Miglyol 812 will be formed.

Interestingly, the higher the concentration of the 98% hydrolyzed PVOH, the less stable became the miniemulsion polymerizations. During reactions with higher PVOH concentrations, 20 wt % and 40 wt % related to the monomer, P3 and P4, particle size increased severely until complete loss of stability (results are not shown here). This lack of stability might be explained by taking into account the high degree of hydrolysis of this PVOH, presenting a high number of hydroxyls ($m = 98\%$ in Figure 1), which contributes for the formation of strong intra- and intermolecular hydrogen bonds. This fact suggests that this PVOH with a high degree of hydrolysis, associated with its hydrophilic characteristic, does not act as stabilizer and affects negatively the colloidal stability.

Carrà et al. evaluated the adsorption isotherms of PVOH onto surfactant-free PVAc particles and observed that the lower the degree of hydrolysis, the greater amount of PVOH adsorbed.¹⁵ The results obtained by these authors might explain the poor stabilization properties of 98% hydrolyzed PVOH observed in Table II, as for instance $N_p/N_m = 0.28$ with 10.0 wt % of PVOH.

When a PVOH with a lower degree of hydrolysis (80%) and lower molar mass (6000 g mol^{-1}) was used as polymeric stabilizer, no noteworthy effect was observed on reaction rate of reactions P5 to P7 with up to 10 wt % of PVOH in relation to monomer [Figure 6(a)]. Reaction P8, though, with the highest PVOH concentration, was faster at the beginning of the

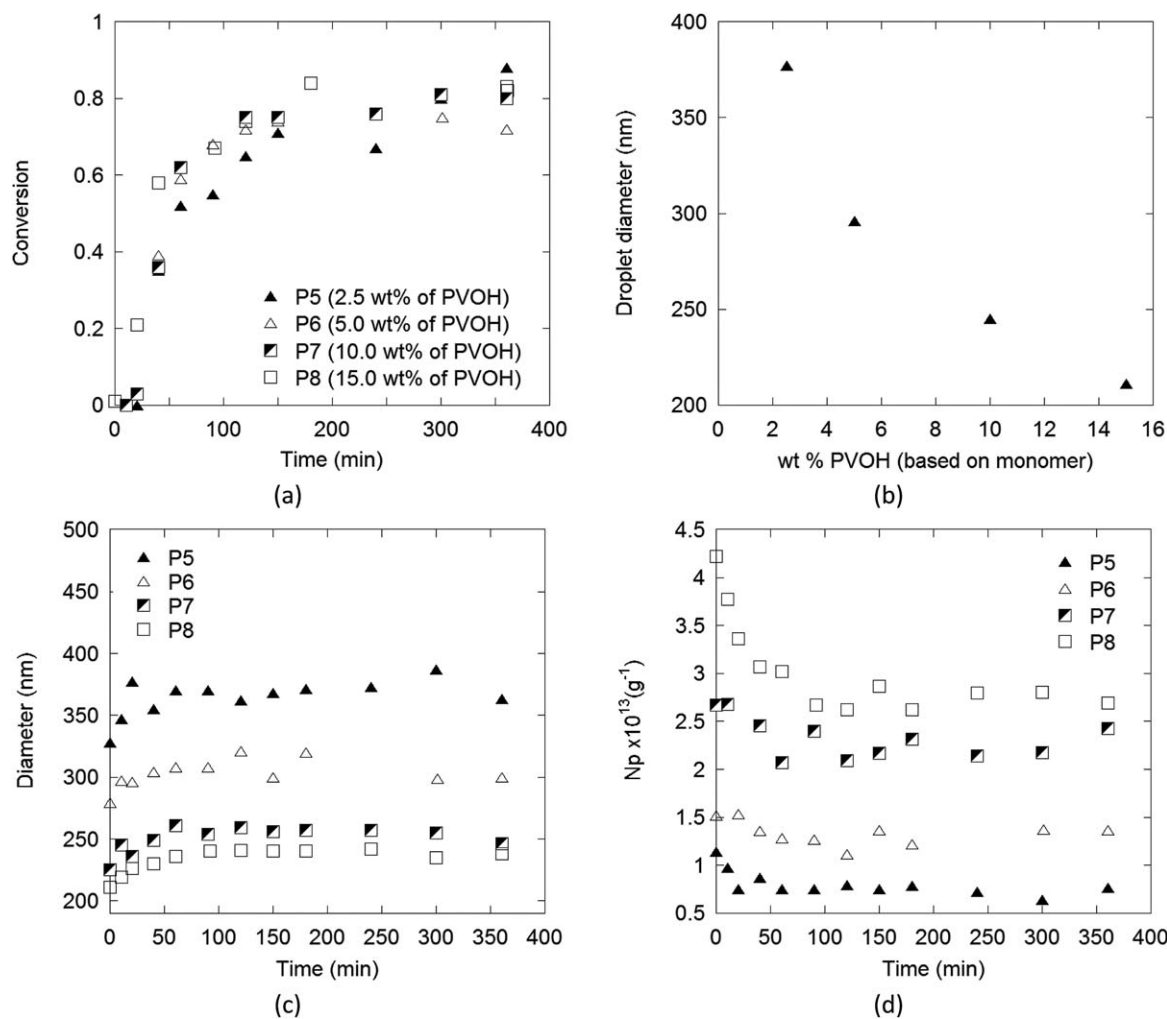


Figure 6. Evolution of properties during VAc miniemulsion polymerizations using PVOH 80% hydrolyzed and 6,000 g mol⁻¹ as polymeric stabilizer. (a) Conversion. (b) Average initial droplet diameters (nm). (c) Average droplet and nanoparticle diameters (nm). (d) Particle numbers (g⁻¹).

reaction. In contrast, initial droplet size strongly depended on PVOH concentration [Figure 6(b)]. A sharp decrease in initial droplet size can be noticed by increasing the PVOH concentration, Figure 6(b). During reactions P5 to P7 with 2.5 to 10.0 wt % of PVOH (80% degree of hydrolysis and molar mass of 6,000 g mol⁻¹) droplet/particle diameters and thus, droplet/particle numbers, remained virtually constant during polymerization. This result indicates that possibly a high fraction of the original droplets was nucleated and that droplets/particles remained stable throughout these reactions.

The values of the ratios between N_p and N_m are provided to contribute on the comparative analysis of the evolution of the droplet/particle number during the polymerization. N_p and N_m ratios around unity indicate that the particle number is close to the initial droplet number, indicating that droplet nucleation was the predominant nucleation mechanism. As shown in Table II, N_p and N_m ratios are close to unity in the reactions with the 80% hydrolyzed PVOH, except for run P8. During reaction P8 with 15 wt % of PVOH (80% degree of hydrolysis and molar mass of 6000 g mol⁻¹), particle diameters increased slightly and, consequently, particle number decreased despite the high

PVOH concentration, resulting in a N_p and N_m ratio value lower than unity. In order to try to elucidate what caused the increase of particle size during reaction P8, the final sample was analyzed by TEM after negative staining with uranyl acetate. TEM images indicate that hemispheres PVAc nanocapsules [Figure 7(a)] formed by droplet nucleation coexist with spherical PVAc particles (around 50 to 100 nm) surrounded by PVOH chains and small PVOH aggregates [5 to 20 nm, Figure 7(d)]. Spherical PVAc particles are believed to be formed by micellar and/or homogeneous nucleation due to the high PVOH concentration of this reaction.

The small PVOH aggregates might be composed of both free PVOH as PVOH-g-PVAc, that form a hydrophobic core by the acetate units surrounded by the hydrophilic vinyl alcohol groups. The ability of PVOH to self-associate by hydrogen bonding is well known. The self-assembly behavior and micellar structure of amphiphilic copolymers depends on chemical composition, total molar mass, among others.²³ Due to the micellar behavior of PVOH-g-PVAc aggregates and their high total superficial area, they might provide the driving force for VAc mass transfer from monomer droplets through the aqueous

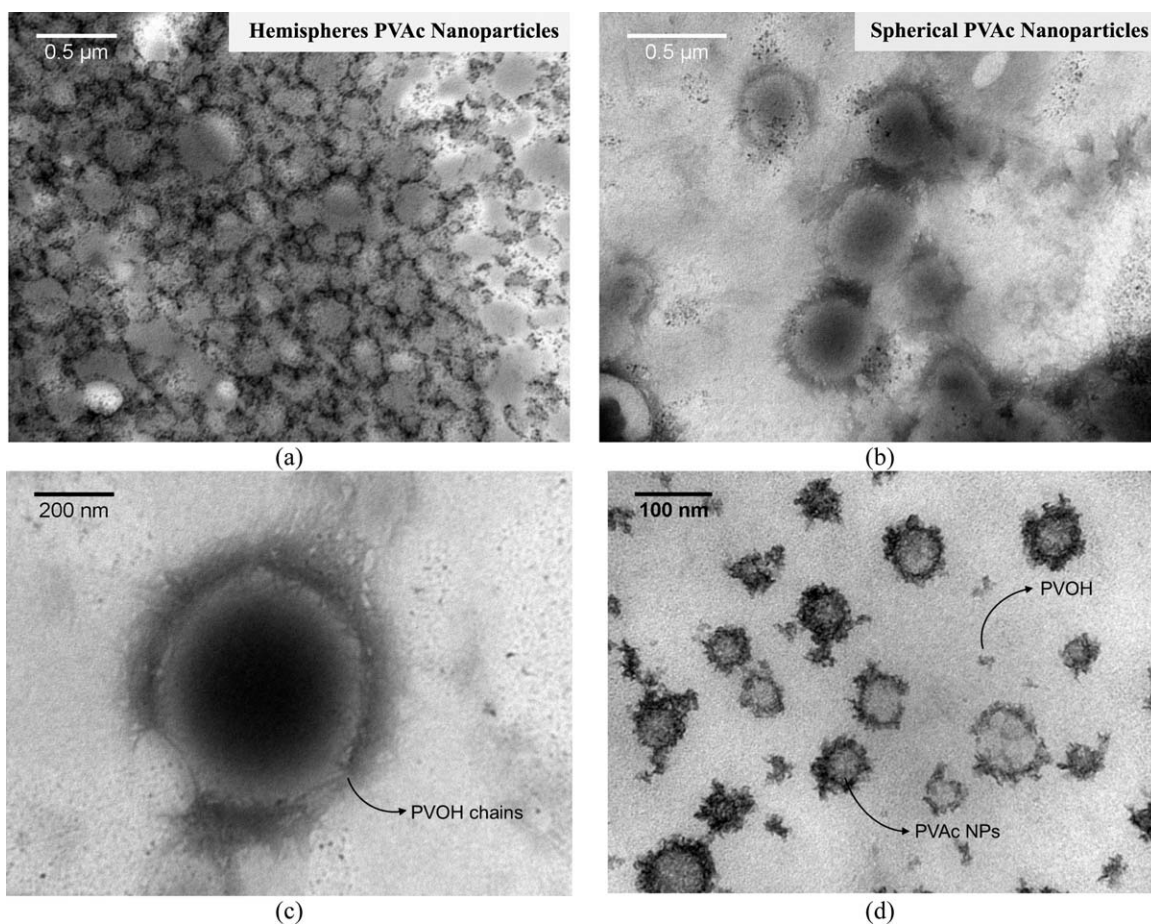


Figure 7. TEM images of final sample P8 stabilized with 15 wt % related to monomer of PVOH 80% hydrolyzed and 6000 g mol^{-1} (negatively stained with uranyl acetate).

phase to the PVOH-g-PVAc aggregates. It must be mentioned that this mass transfer is favored by the relatively high solubility of VAc in the aqueous phase ($0.32M$ at 50°C).²² In addition, since an oil soluble initiator (AIBN) was used in these reactions, radicals that enter the PVOH aggregates are either from the small initiator fraction that is soluble in the aqueous phase or initiator radicals or unitary monomer radicals formed due to the high chain transfer rate to monomer. This result is in good agreement with those of Bohórquez et al., who observed that high PVOH concentrations may lead to micellar nucleation during VAc and VeoVa 10 miniemulsion copolymerizations.¹ The higher particle number at the initial stages of reaction P8 might also contribute to the higher rate of this reaction [Figure 6(a)].

The decrease of the particle number during reaction P8 [Figure 6(d)] is probably due to the coalescence of the small particles formed by micellar and/or homogeneous nucleation with the original miniemulsion droplets/particles, in a similar way as often observed during conventional batch VAc emulsion polymerization.

Nanoparticles prepared with 15.0 wt % of PVOH (88% hydrolyzed PVOH and $M_w = 78,000 \text{ g mol}^{-1}$) were also investigated according to its final morphology (reaction P9). Results shown in Figure 8 indicate that the predominant morphology is indeed hemisphere nanoparticles and that the grafted and/or adsorbed

PVOH chains on the particle surface tend to form clusters. In order to verify if the structure formed by PVOH is three-dimensional, different incident angles of electron beam over the grid during the TEM analysis were analyzed, Figure 9, and the three-dimensionality was confirmed, as emphasized by arrows 1 and 2.

Although the weight amount of PVOH in reaction P9 is equal to that of reaction P8, small aggregates/micelles of PVOH were not seen during the analysis of sample P9, due to the lower molar concentration of PVOH in reaction P9. Additionally, miniemulsions prepared with 88% hydrolyzed PVOH with $M_w = 78,000 \text{ g mol}^{-1}$ present a higher viscosity of the continuous aqueous phase. Figure 10 shows the relative viscosities of the aqueous phase composed of different concentrations of two types of PVOH, one with low molar mass (P5 to P8) and another with a high molar weight (P10 to P12). It is already established that higher viscosity turns stirring and thus homogeneous droplet breakage during miniemulsion preparation more difficult.^{1,4} According to Asua, a problem associated with sonifiers is that only a small region of the fluid around the sonifier tip is directly affected by the ultrasound waves.⁴ Although additional stirring was used during the sonication step to allow all the fluid to pass through the sonication region, nanoparticles size was slightly larger than 300 nm and broad size distribution for reaction P9.

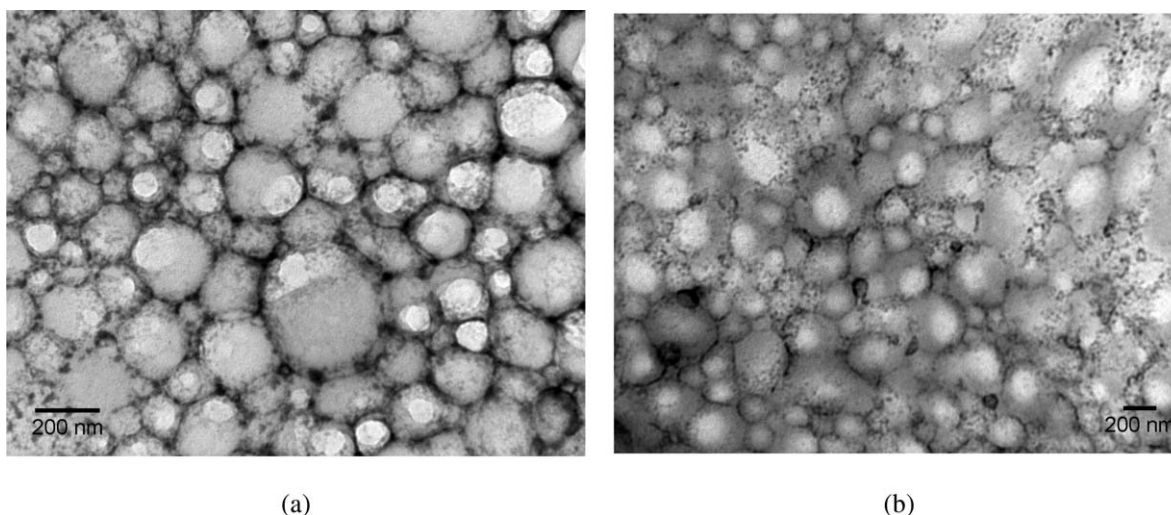


Figure 8. TEM images of final sample P9 stabilized with 15 wt % related to monomer of PVOH 88% hydrolyzed and $78,000 \text{ g mol}^{-1}$ (negatively stained with uranyl acetate). a) Carbon coated cooper grid. b) Parlodium coated cooper grid.

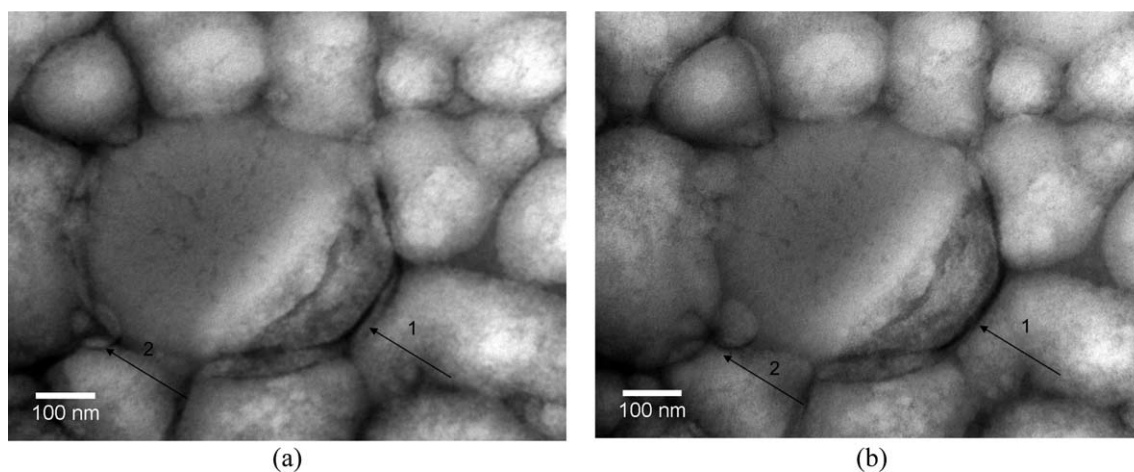


Figure 9. TEM images of final sample P9 stabilized with 15 wt % related to monomer of PVOH 88% hydrolyzed and $78,000 \text{ g mol}^{-1}$ (negatively stained with uranyl acetate) with different incident angles of electron beam over the grid (a) -20° (b) $+20^\circ$.

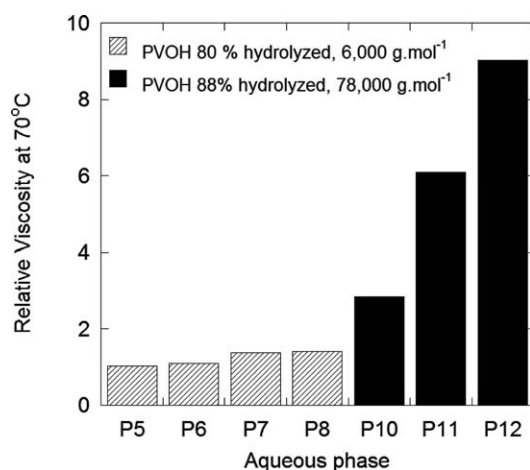


Figure 10. Relative viscosity of the aqueous phase of miniemulsions P5 to P12 with different PVOH types and concentrations measured at 70°C .

To overcome these facts, the sonication procedure was investigated and the time was increased from 4 to 8 min. The effect of sonication time is shown in Figure 11 and it can be observed that longer sonication time decreased the initial average droplet diameter from 306 nm (P9) to 296 nm (P10). On the other hand, according to Bohórquez et al., PVOH may improve the stability of miniemulsions due to the higher viscosity of the continuous phase.¹ This effect can be observed for diameter evolution during polymerization P10, Figure 11(b).

According to the results presented, the following polymerizations were performed applying sonication time for 8 min. The evolution of properties during VAc miniemulsion polymerizations using PVOH 88% hydrolyzed and $78,000 \text{ g mol}^{-1}$ as polymeric stabilizer are shown in Figure 12. No significant effect was observed in the reaction rate, Figure 12(a), although, the initial droplet size decreased with the increase of the amount of PVOH and then achieved a constant value that

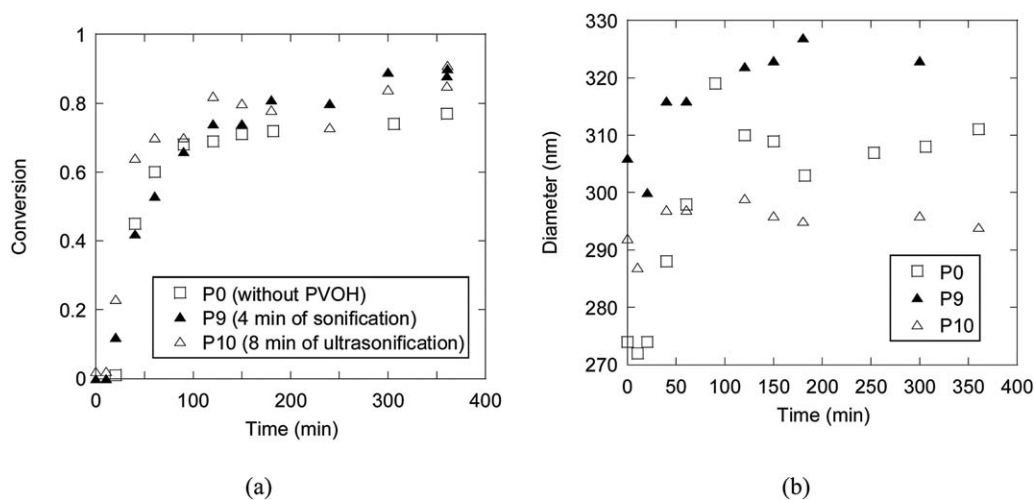


Figure 11. Evolution of properties during VAc miniemulsion polymerizations using PVOH 88% hydrolyzed and $78,000 \text{ g mol}^{-1}$ as polymeric surfactant. (a) Conversion. (b) Average droplet and nanoparticles diameters (nm).

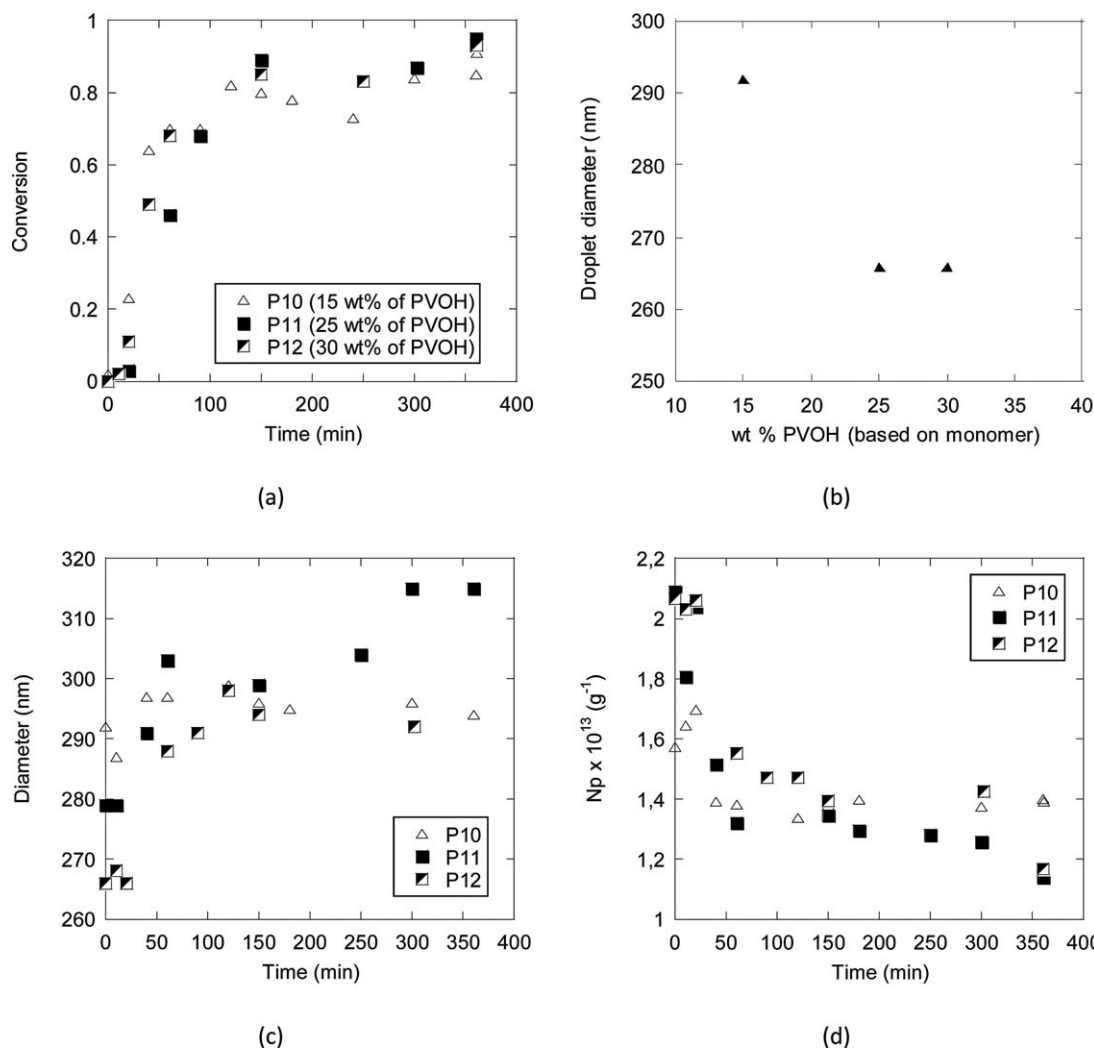


Figure 12. Evolution of properties during VAc miniemulsion polymerizations using PVOH 88% hydrolyzed and $78,000 \text{ g mol}^{-1}$ as polymeric surfactant. (a) Conversion. (b) Average initial droplet diameters (nm). (c) Average droplet and nanoparticles diameters (nm). (d) Particles numbers.

did not depend anymore on the PVOH concentration, Figure 12(b), similar to the results observed by Bohórquez et al. and Kim et al.^{1,12} These authors observed that droplet size decreased exponentially with PVOH concentration and then leveled off, indicating that there was enough PVOH to stabilize these droplets and PVOH molecules started to buildup in the aqueous phase favoring the occurrence of micellar and/or homogeneous nucleation. These results evidence the excess of PVOH in the miniemulsion and, shift of the predominant nucleation mechanism might occur.

According to results shown in Figure 12(c), the increase of particle diameters during polymerization (reactions P11 and P12) might be explained taking into account the excess of PVOH in the continuous phase. The formation of new particles by homogeneous and/or micellar nucleation favors coalescence as discussed before, consequently, decreasing the particle numbers during polymerization reaction, Figure 12(d). Reaction P10, with a lower amount (15 wt %) of 88% hydrolyzed and 78,000 g mol⁻¹ PVOH, on the other hand, resulted in more constant values of D_p and N_p throughout the polymerizations.

CONCLUSIONS

High oil content was incorporated in PVAc nanoparticles stabilized by PVOH (different types and concentrations). The nanoparticles were synthesized by batch miniemulsion polymerizations using biocompatible surfactants and co-stabilizer, resulting in final hemisphere nanoparticles morphology. It was observed that for PVOH to act as an efficient polymeric surfactant, the hydrolysis degree is an important parameter. When 98% hydrolyzed PVOH was used, particle size increased considerably during polymerizations and particles with a broad size distribution were obtained. When, on the other hand, PVOH with a lower degree of hydrolysis was used droplet nucleation could be maximized and optimal PVOH concentration to provide stable nanoparticles was 2.5 to 10 wt % of 80% hydrolyzed and 6000 g mol⁻¹ PVOH and 15 wt % of 88% hydrolyzed and 78,000 g mol⁻¹ PVOH. Higher concentrations of both PVOH types led to new particle formation by micellar particle nucleation.

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