Influence of the Geometric Factors of the Experimental Device Used in Suspension Polymerization on the Properties of Poly(styrene-*co*-divinylbenzene) Microparticles

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ABSTRACT: The prediction of the final particle size for reactive systems such as the reactions of suspension polymerization is a complex matter. Thus, the preparation of very small microparticles is specially challenging, probably because of the coalescence of the polymeric beads taking place during the later stages of the polymerization. In this work, very small gel-type styrene-*co*-divinylbenzene beads were synthesized by using a previously determined set of experimental synthesis conditions in which the stabilization of the dispersion of the monomeric droplets was ensured, and, under these conditions, the factors related to the geometry of the experimental device were modified to determine their actual effect on the final size of the microparticles. From the experimental results, a very simple and useful model was obtained that was able to predict the final size of the microparticles as a function of the values of the geometric factors of the reactor. This model indicates that the most influential factors in the final size of the microparticles are the liquid depth inside the reactor and the stirrer diameter; thus, an increase in the liquid depth produces larger particles, and, conversely, the particle size decreases when using larger stirrer diameters. Additionally, the model permits the design of polymerization experiments aimed at obtaining microparticles with a diameter smaller than 50 μm. © 2011 Wiley Periodicals, Inc. J Appl Polym Sci 124: 1431–1446, 2012

Key words: polymerization; particle size distribution; morphology; polystyrene; geometric factors

INTRODUCTION

Polymeric microbeads have many applications, most of them related to the adsorption phenomenon, such as in ion exchange,[1,2] as packing materials in chromatographic columns,[3] as catalyst supports,[4] in solid-phase extraction,[5] in solid-phase synthesis,[6,7] and in combination with magnetic material.[8,9] Owing to their excellent mechanical and chemical properties, polystyrene-based microbeads are one of the most widely used materials as supports of polymer-based adsorbents.[10,11] This kind of microparticle is usually obtained by free radical crosslinking copolymerization of styrene and divinylbenzene monomers using the suspension polymerization technique, with divinylbenzene as the crosslinker.[12–14]

With regard to the properties of the microbeads obtained with this technique in relation to their size, it must be emphasized that their mean size and their size distribution are significant characteristics regarding their applications, and, consequently, control of these aspects is one of the most important aims of suspension polymerization technology.[12–14] This is because the size distribution should be as narrow as possible to facilitate the use of the product,[15] and because the optimum particle size may be different, depending on the application in which the beads are to be used. For instance, very small microparticles have the advantage of reducing problems due to the slow diffusion of fluids into them.

In addition to their size, the final morphology of the microparticles is also an important characteristic of microparticles with regard to their applications.[12,16] Thus, the methodology of suspension polymerization processes should enable the process to be guided toward the production of nonaggregated spherical microparticles and also toward the achievement of the intended particle size distribution (PSD). However, this is not easy because, in fact, all these characteristics are interrelated. Thus, in the case of monomeric liquid droplet size, this

property mainly depends on the geometric factors of the experimental device and on other factors related to the operation conditions, such as the stirring rate and the physical properties and proportions of certain substances used during the polymerization process, such as surfactants and the suspension agents. These substances are used to stabilize the dispersion by affecting the rates of breakage and coalescence of the droplets during the early and intermediate stages of the polymerization process. Accordingly, these factors also affect the morphology of the beads and their PSD, because owing to the progressive increase in the conversion of the monomers, the division of the droplets becomes more difficult, and, after a certain reaction time, the coalescence rate may exceed the break-up rate, and the mean size of the droplets could rise. Moreover, it is likely that the forces exerted by turbulence could deform the highly viscous droplets permanently or even that incomplete coalescence processes could produce clusters of particles. Therefore, the design of experiments addressed to obtain a given final particle size, in the case of reactive systems such as polymerization reactions in suspension, is challenging, because it is very probable that during the intermediate and final stages of the polymerization processes, the agglomeration and deformation of the droplets/particles will vary the original liquid droplet size distribution and mask the real influence of the above experimental factors on that distribution.[14,17]

However, in spite of the complexity of the processes that occur throughout the polymerization reaction, several models[12,13,15,18,19] with different degrees of complexity have been developed that attempt to take into account the effects of the geometry of the reactor, the type of mixing of reactants, and even the kinetics of polymerization on particle size. Thus, Arshady[20] has reported an empirical relationship whose aim is to represent most of the results obtained earlier by combining the values of the synthesis conditions and those of certain geometric factors of the experimental device to predict the mean size of the microparticles. Unfortunately, although these models are a helpful guide for planning new suspension polymerization experiments, they cannot be considered a complete solution of the problem for one or more of the following reasons: (a) to solve the models, it is necessary to know the values of variables that are not only hard to know but that also usually change along the process, such as the viscosity of the dispersed phase or the interfacial tension; (b) the solution of most such models is not straightforward; and (c) models have been derived from experimental data obtained in polymerization reactions, in which microparticles with a size larger than 100 µm were synthesized.

Actually, in spite of the important applications of very small microparticles, there is a lack of models

aimed at facilitating their synthesis. This may be due to the fact that the preparation of very small microparticles is more complex, probably as a result of the distorting effect on their size caused by the coalescence of the polymeric beads that occurs during the later stages of polymerization. Taking this problem into account, and looking for a solution, it seems appropriate to bear in mind that in the first stage of suspension polymerization, the formation of a dispersion of monomeric droplets in water occurs due to the stirring, and this is followed by direct conversion of the monomer droplets into the corresponding polymeric solid beads due to the effects of heat and of the catalyst. In this scenario, an ideal situation would be that the final size distribution of the solid polymeric beads should be similar to that of the monomeric droplet size distribution achieved in the initial stages of polymerization as a result of the stirring of the reaction mixture. This ideal situation may seem unrealistic, but, in fact, it could be achieved through stabilization of the dispersion by using an appropriate combination of the values of the geometric factors and of the operating conditions, and this stabilization seems to be the only way to study the true influence of any experimental factor on the final PSD in a polymerization system, because the individuality of the droplets/particles and their spherical shape throughout the polymerization reaction should be preserved.

The advantage of accomplishing this stabilization would be the possibility of estimating the final size of the microparticles using correlations originally addressed to the prediction of the very small final size of liquid droplets in immiscible liquid–liquid dispersions. At this regard, many authors have reported studies addressing immiscible liquid–liquid dispersions in stirring tanks in which the mean droplet diameter and its distribution were related to the experimental conditions used.[17,21–27] Nevertheless, all these studies were carried out using unreactive mixtures, and there are no studies that have addressed the application of these relationships to suspension polymerization.

Within this field of research, in an earlier work,[28] we reported a thorough investigation of the influence on the morphological characteristics of the final solid polymeric microparticles, of certain factors related to the synthesis conditions, and the values of the factors at which the stabilization of the dispersion persisted throughout the suspension polymerization process were determined. Here, continuing along this avenue of enquiry, we have performed an investigation aimed at studying the effects of the geometric factors of the experimental device on microparticle size and on their size distribution in which one requirement was to maintain the quality of the microparticles as regards agglomeration and

sphericity. The general objective of this research was to check the applicability of relationships obtained for unreactive stirred liquid–liquid systems to suspension polymerization processes to facilitate the design of experimental devices aimed at obtaining polymeric particles with a suitable shape and a wide range of sizes, especially very small particles. Specifically, the aims of this research were (a) to determine the existence of geometric factors that may have a significant influence on the final microparticle size without affecting their quality with regard to sphericity and agglomeration; (b) to find a quantitative relationship between those influencing geometric factors and the mean size of the microparticles, based on dimensionless models employed in dispersions of immiscible liquids, which is useful for the design of experiments aimed at the synthesis of very small microparticles. To achieve this objective, the research was planned with the factorial design of experiments methodology to find the effects of the geometric factors on the response, and determination of the relationship was carried out using multiple linear regression analysis. The characterization of the product was carried out by laser diffraction, in the case of determining the PSD, and by microscopy, in the case of the agglomeration and sphericity of the microparticles.

EXPERIMENTAL

Materials

Organic phase

Commercial styrene (St, 99%) and divinylbenzene (DVB, containing 55% DVB isomers, the remainder mainly being 3- and 4-ethylvinylbenzene), supplied by Aldrich (Madrid, Spain), which were used as monomers, were first washed with a 10% NaOH aqueous solution to remove inhibitor, *p-tert*-butylcatechol, and then with deionized water until neutralization. The polymerization initiator, benzoyl peroxide (70%, remainder water), was supplied by Aldrich (Madrid, Spain) and used as received.

Aqueous phase

Anhydrous calcium chloride (95%), 1-hydrated sodium triphosphate (98%), and ammonium hydroxide solution (32%) were supplied by Scharlau (Barcelona, Spain). Sodium dodecyl sulfate (SDS, 85%) was obtained from Panreac (Barcelona, Spain). All these substances were used without further purification. Deionized water was used to prepare the aqueous solutions.

Synthesis of gel-type polymeric microparticles procedure

Gel-type poly(St-*co*-DVB) microparticles were synthesized with the suspension polymerization technique, using tricalcium phosphate (TCP) as the suspension agent. TCP was prepared *in situ* by mixing solutions of anhydrous calcium chloride and 1-hydrated sodium phosphate. The aqueous phase also contained ammonium hydroxide to enhance the protective properties of the suspension agent and SDS to decrease the interfacial tension. The reaction was performed in a three-necked round-bottomed jacketed glass reactor fitted with a mechanical stirrer, a reflux condenser, and a thermocouple. The organic phase was dispersed in the aqueous phase by stirring at 900 rpm, and this stirring rate was maintained for 3 h at room temperature to ensure that the average size of the monomer droplets would reach a constant value. This long period of stirring of a dispersion, at room temperature, is justified considering that we were attempting to find a quantitative relationship between the final size of the microparticles and the values of the geometric factors of the experimental device and that this is only possible if the polymerization starts from monomeric droplets with a stationary mean size that depends only on the stirring rate and on the geometric characteristics of the experimental device. Moreover, this stationary size is the minimum size achievable for the experimental conditions used. This size of the droplets was checked by collecting samples from the reactor at different times and scrutinizing them by light microscopy. Following this, to preserve the small size attained by the droplets, ammonia was added to the reactor to ensure the existence of a basic pH in the polymerization mixture and hence maintain the protective properties of TCP against the coalescence of the droplets. Next, the temperature inside the reactors was increased to 80°C to start the polymerization reaction and kept at this value for 7 h. Nevertheless, the stirring rate was not held constant throughout the polymerization reaction, but was decreased after a certain polymerization time. This approach can be justified taking into account the mechanisms of breakage and coalescence of the monomeric droplets. In the early stages of polymerization, the monomeric droplets are very fluid and can be broken by the effect of the turbulences caused by stirring, and they may also coalesce due to the effect of collisions between them. However, as polymerization proceeds, the monomeric droplets become more viscous, and their breakage, as a result of stirring, is less common. This is not the case with coalescence, because highly viscous droplets are still able to coalesce, because the protective layer of TCP is not always completely effective. Consequently, it was decided that, once a certain degree of viscosity had been reached, it would not be necessary to maintain a high rate of stirring, because this does not serve to break the droplets, and, conversely, it could promote their coalescence. Experimentally, the

proper viscosity was found at ~ 1.3 h after the start of polymerization, and hence, at that time, the stirring rate was reduced to 550 rpm, which was high enough to keep the monomeric droplets dispersed but low enough for collisions to occur without coalescence. Additionally, to ensure the stabilization of the dispersion throughout the suspension polymerization process, the values of the synthesis conditions given in Table I were selected to obtain microparticles with optimized morphological characteristics.[28,29] Details of the polymerization procedure have been reported previously.[28]

Characterization of microparticles

The microparticles were characterized by measuring their PSD and by studying their morphology. The PSD was measured by means of laser diffraction on a Malvern Mastersizer 2000 device. Analysis of their morphology was performed by light microscopy, with a ZUZI 172 light microscope, and their surface topography was investigated by scanning electron microscopy (SEM) using a Zeiss DSM 940 scanning electron microscope.

Design of experiments

The research was first planned through a factorial design of experiments.[30,31] In this way, the factors with statistical influence on the responses can be determined. To apply this methodology, a sequence of steps must be followed:

Problem identification

An ideal suspension polymerization process should produce individual spherical particles with a controllable size and a size distribution as narrow as possible, because this is the major aim in this kind of polymerization.[12–14] Therefore, it would be desirable to have available quantitative relationships between the characteristics related to the size and morphology of the microparticles obtained and the experimental conditions of the suspension polymerization used in their synthesis. In fact, as stated earlier, there is a lack of reported experimental works focused on obtaining polymeric particles smaller than 100 μm. However, to obtain correlations that link particle size and the experimental parameters, the resulting product must have adequate morphological properties, because if the particles are not spherical or are agglomerated, their average size, or the breadth of their size distribution, will not be directly related to the experimental conditions. Thus, the first problem that arises is to find a region of values of operating conditions in which the stabilization of the dispersion throughout the polymerization

TABLE I
### Values of the Experimental Conditions That Were Kept Constant in All the Experiments

Substances	Proportions
Organic phase, OP (% regarding organic phase volume)	
Styrene	90%
DVB	5.5%
Ethylvinylbenzene	$\sim 4.5\%$
BPO	4% (w/v)
Aqueous phase, AP (% regarding aqueous phase volume)	
Deionized water	100%
TCP	1.4% (w/v)
Volume (mL)	150
OP/AP	1/6 (v/v)
SDS	0.01% (w/v)
NH$_4$OH	0.8% (v/v)
Impeller off bottom clearance	$0.1 \cdot D^a$

[a] See Table II.

process is achieved, because only in this case will the size of the final solid polymeric microparticles be very similar to that of the monomeric droplets formed during the first stage of the polymerization.[14,32] Once this requirement has been achieved, the main aim is to determine the effects of the geometric factors of the experimental device on the mean of the PSD. After these effects have been established, the next problem is to determine quantitative relationships between the influential variables and the properties of the microparticles related to their size to facilitate the design of suspension polymerization processes oriented at obtaining microparticles with predetermined properties.

Factor identification

The suspension polymerization process has been widely studied.[12–14,16,20,33,34] Many experimental factors have an effect on the morphological properties and on the size of the microparticles synthesized. However, once a set of values of synthesis conditions that lead to optimal morphologic characteristics of the microparticles (Table I) has been established, the following task is to study the effects of the geometric factors of the experimental device on the properties related to the size of the microparticles obtained. These factors have an effect on the power input to the polymerization mixture due to stirring[35] and also on the distribution of this power through the polymerization mixture. Thus, they have a fundamental influence on the mean size of the microparticles achieved.[36] This influence can be explained in terms of the notion that the break-up of the organic phase into small droplets, which are dispersed in the continuous phase at the beginning of the polymerization process, is originated by the turbulences
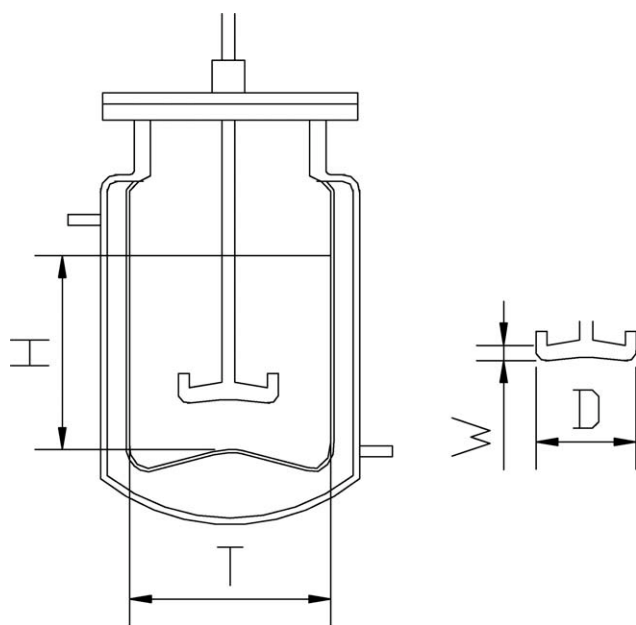
Figure 1 Diagrams of the reactor and of the stirrer used and the variables used as factors in this work.

in the continuous phase caused by the rotation of the blades of the stirrer. The magnitude of these turbulences depends on the stirring speed, on the size of the blades of the stirrer, and also on the volume of the polymerization mixture, because the larger the volume to be stirred, the lower the average energy of the turbulences. Consequently, in this investigation, both the geometry of the blades of the agitator and the volume of the mixture of polymerization were considered as factors having a potential effect on the final size of the particles.

Thus, the factors studied (Fig. 1) are given below.
Polymerization mixture volume. This variable is represented by the product of the values of the reactor diameter (T) and of the liquid depth inside it (H). This factor is related to the volume of the polymerization mixture, and it has an effect on the local intensity of the energy, and, as a consequence, it has a potential effect on droplet size.[36,37]
Stirrer diameter (D). This is the most influential variable of all those related to the stirrer geometry. It has an important effect on the flow regime and on the power input due to stirring.[35] Thus, it has a crucial influence on the final drop size.[24,36–39]
Width of stirrer blades (W). This factor has an effect on the height of the impeller zone, because the wider the blade, the higher the pumping capacity of the impeller, and the larger the zone with turbulences capable of breaking up the droplets.[40] Furthermore, because the pumping capacity is directly related to the power number,[36] the power number is related to this factor, and, therefore, it may affect the droplet size achieved.

Level identification

After trying different types of stirrers,[41] it was decided to study the effect on the responses of the geometric factors of the stirrer and the reactor displayed in Figure 1. The real and the coded values of the levels of the factors are given in Table II.

Response identification

The main objective of this research was to determine the quantitative effect of the geometric factors of the polymerization device on the size of the polymeric microparticles obtained. Thus, because the most representative parameter of this size is the mean of the PSD curves (by volume), d_{50}, this parameter was the main response to be measured. Moreover, the sphericity, the agglomeration of the microparticles, and the breadth of the PSD were also considered as responses. The agglomeration and the sphericity indices were also included as responses.[42] The measurement of the degree of both agglomeration and sphericity was quantified by an index. The first step to ascribe a value to the indices of both agglomeration and sphericity was to carry out a qualitative valuation. Hence, some qualitative features that are related to both agglomeration and no-sphericity were established. The features of the microparticles included under the term agglomeration were microparticles with "satellites" (very small beads affixed to the surface of larger particles); microparticles with "warts" (agglomerations of small beads affixed to the surface of larger particles); "dirty" microparticles (microparticles with small irregularly shaped portions of polymer affixed to their surface) and clusters (agglomerated particles). Regarding the term sphericity, the features selected were elongated (microparticle with an unbalance ratio of its axis), oval shape (microparticle with an oval shape), and irregular (microparticle with a nonspecific shape different from the spherical one and the previous ones). To obtain a quantitative evaluation of the degree of agglomeration and sphericity, three samples were taken from each experiment and each was divided into 10 portions. All the portions were inspected under light microscopy (Fig. 2). If in a portion at least one particle displayed one of the above-

TABLE II
Levels of the Factors Used in the First Set of Experiments

Factor	Term	Low level (−1)	High level (+1)
Polymerization mixture volume (cm^2)	TH	33.6	75.1
Stirrer diameter (cm)	D	4.6	5.8
Width of stirrer blades (cm)	W	0.7	1.1
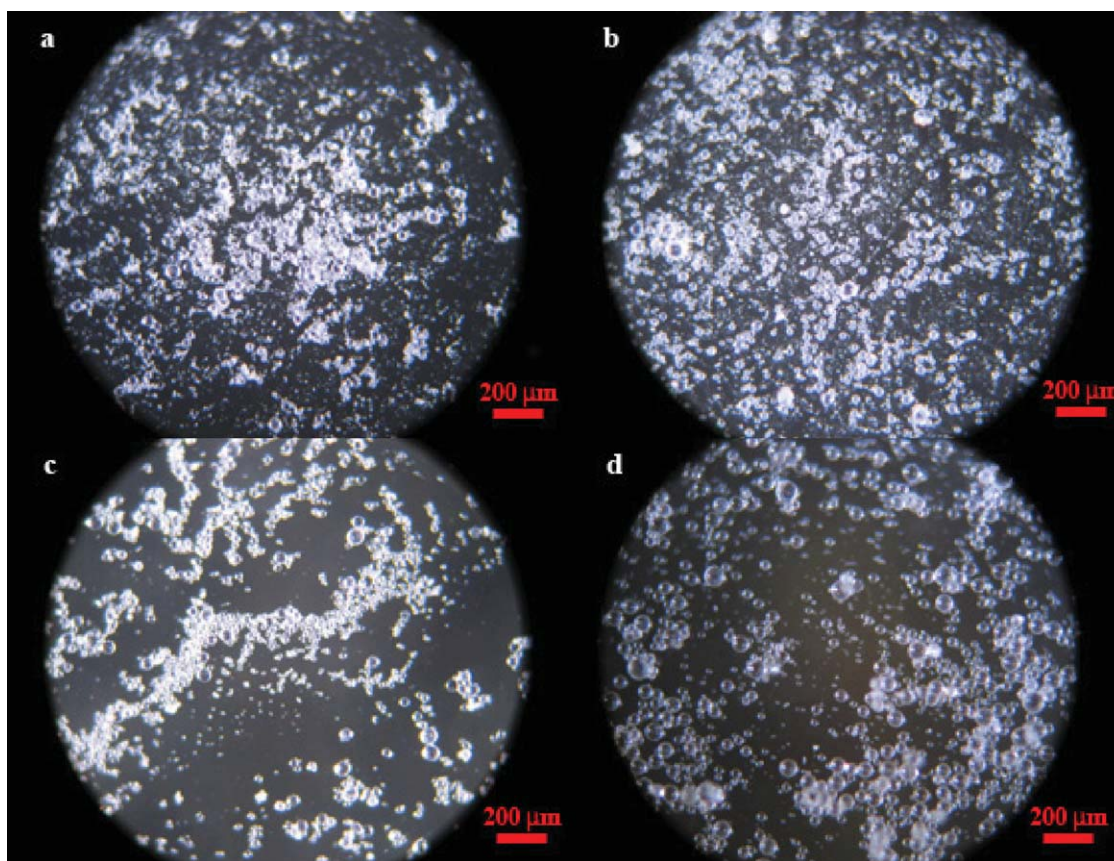
Figure 2 Light microphotographs of microparticles obtained with reflected light. The pictures correspond to microparticles of (a) experiment 7; (b) experiment 10; (c) experiment 13; (d) experiment 14. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

mentioned features, it was assigned one point (1) in that feature; otherwise, it was valued with a zero (0). To calculate the agglomeration and sphericity indices, eqs. (1) and (2) were used, respectively. Under this procedure, when the agglomeration and nonspherical features are not very prominent, it is considered that the microparticles have good quality, and, consequently, the better the quality of microparticles the closer to unity are the values of their indices of agglomeration and sphericity.

$$\text{Agglomeration index} = 1 - \frac{N^{o}_{\text{Satellites}} + N^{o}_{\text{Warts}} + N^{o}_{\text{Dirties}} N^{o}_{\text{Clusters}}}{N^{o}_{\text{Features}} \cdot N^{o}_{\text{Portions}}} \quad (1)$$

$$\text{Sphericity index} = 1 - \frac{N^{o}_{\text{Elongated}} + N^{o}_{\text{Oval}} + N^{o}_{\text{Irregular}}}{N^{o}_{\text{Features}} \cdot N^{o}_{\text{Portions}}} \quad (2)$$

where N^{o}_{x} is the number of portions with the x feature, and N^{o}_{Features} is equal to 4 for the agglomeration index and 3 for the sphericity index, and N^{o}_{Portions} is 10.

The analysis of the agglomeration and sphericity indices was carried out to verify the stability of the dispersion in all the experiments, because it could

be objected that the assumed optimum values of the synthesis conditions, summarized in Table I, were determined by employing only a given set of values of the geometric factors of the experimental device. Under these circumstances, it may be surmised that if the values of these geometric factors were modified, some type of interaction could occur between the synthesis conditions and the new geometry of the reaction device, leading to the destabilization of the polymerization system, and hence to decreased product quality. Therefore, taking into account that it would be very difficult to determine the true effect of geometric factors on the size of polymeric particles in the event that, by modifying the values of the geometrical factors of the experimental device, the best synthesis conditions were different, in addition of studying the particle size, it was also necessary to check that their agglomeration and sphericity maintained their appropriate values in all experiments. Thus, the agglomeration and sphericity of the microparticles were quantified by determining their indices,[42] and the quantitative effect of the geometric factors of the polymerization device on these microparticle characteristics was calculated. Additionally, because

TABLE III
Design Matrix: Level of the Factors and Response Values

	Factor levels										
	\multicolumn{4}{c}{Polymerization mixture volume (TH)}				\multicolumn{2}{c}{Stirrer diameter (D)}		\multicolumn{2}{c}{Width of stirrer blades (W)}		\multicolumn{4}{c}{Response values}
Exp. number	T (cm)	H (cm)	Real value (cm^2)	Coded value	Real value (cm)	Coded value	Real value (cm)	Coded value	Agglomeration Index	Sphericity Index	d_{50} (µm)	Span
1	7.0	4.8	33.6	−1	4.6	−1	0.7	−1	0.88	0.87	39.61	1.26
2	9.25	8.1	75.1	+1	4.6	−1	0.7	−1	0.85	0.83	49.49	1.19
3	7.0	4.8	33.6	−1	5.8	+1	0.7	−1	0.90	0.93	20.71	1.97
4	9.25	8.1	75.1	+1	5.8	+1	0.7	−1	0.90	0.90	28.76	1.54
5	7.0	4.8	33.6	−1	4.6	−1	1.1	+1	0.88	0.83	32.80	1.76
6	9.25	8.1	75.1	+1	4.6	−1	1.1	+1	0.90	0.87	43.34	1.22
7	7.0	4.8	33.6	−1	5.8	+1	1.1	+1	0.88	0.87	25.64	1.89
8	9.25	8.1	75.1	+1	5.8	+1	1.1	+1	0.85	0.87	36.91	1.31
9	7.0	4.8	33.6	−1	4.6	−1	0.7	−1	0.80	0.85	33.84	1.44
10	9.25	8.1	75.1	+1	4.6	−1	0.7	−1	0.90	0.83	34.95	1.38
11	7.0	4.8	33.6	−1	5.8	+1	0.7	−1	0.85	0.83	21.53	1.29
12	9.25	8.1	75.1	+1	5.8	+1	0.7	−1	0.90	0.90	34.84	1.34
13	7.0	4.8	33.6	−1	4.6	−1	1.1	+1	0.88	0.90	33.68	1.40
14	9.25	8.1	75.1	+1	4.6	−1	1.1	+1	0.88	0.87	53.21	1.17
15	7.0	4.8	33.6	−1	5.8	+1	1.1	+1	0.83	0.80	29.22	1.16
16	9.25	8.1	75.1	+1	5.8	+1	1.1	+1	0.88	0.87	25.21	1.62

another representative characteristic of the size of the particles is their PSD, it was decided to study the breadth of the PSD by determining the span response, defined by eq. (3):

$$\text{span} = \frac{d_{90} - d_{10}}{d_{50}} \qquad (3)$$

where d_{90} indicates the diameter for which 90% of the particles in the sample are smaller than that diameter, the meaning of the parameters d_{10} and d_{50} being analogous.

Planning of experiments

The research was initially planned as a trifactorial design with eight experiments and their replicates, as shown in Table III, which were carried out with the values of the synthesis conditions shown in Table I.

RESULTS AND DISCUSSION

Light microscopy and SEM analyses

Light microscopy was used to study the morphology of the microparticles and to determine the agglomeration and sphericity indices. As may be observed in Figure 2, the microparticles from all the experiments were spherical and free of clusters indicating the high quality of the microparticles obtained with respect to these properties. According to the results of the light microscopy analysis of the experiments, it may be assumed that dispersion had been stabilized in all the experiments and, consequently, that no interactions had occurred, between the synthesis conditions and the geometric factors, able to produce an agglomeration or deformation of the microparticles. Likewise, the high quality of the microparticles with regard to agglomeration and to sphericity suggests that the size of the solid polymeric particles obtained was similar to that of the liquid droplet size reached in the dispersion of the immiscible liquid–liquid system at the beginning of the polymerization process. Thus, an initial conclusion would be that according to the results of the experiments, it would be possible to study the real effect of the geometric factors of the experimental device on the final polymeric PSD. In addition, it may be seen in Figure 2 that the microparticles are not opaque, this being a characteristic of gel-type microparticles owing to their homogeneous structure. Moreover, with the scale bar, it is possible to estimate the size of the microparticles, most of them being smaller than 100 µm.

Microparticle topography was studied with SEM, and microphotographs from experiments 12 and 18 (see section "Additional Experiments") are shown in Figure 3, in which it can be observed that the microparticles are spherical and free of agglomeration. Thus, the microphotographs obtained by this technique corroborated the conclusions drawn after analyzing the light microphotographs. In the case of experiment 18 [Fig. 3(b)], there are very small microparticles on the surface of larger microparticles, although this cannot be considered a sign of agglomeration, because the union between these particles does not seem to correspond to chemical bonding;
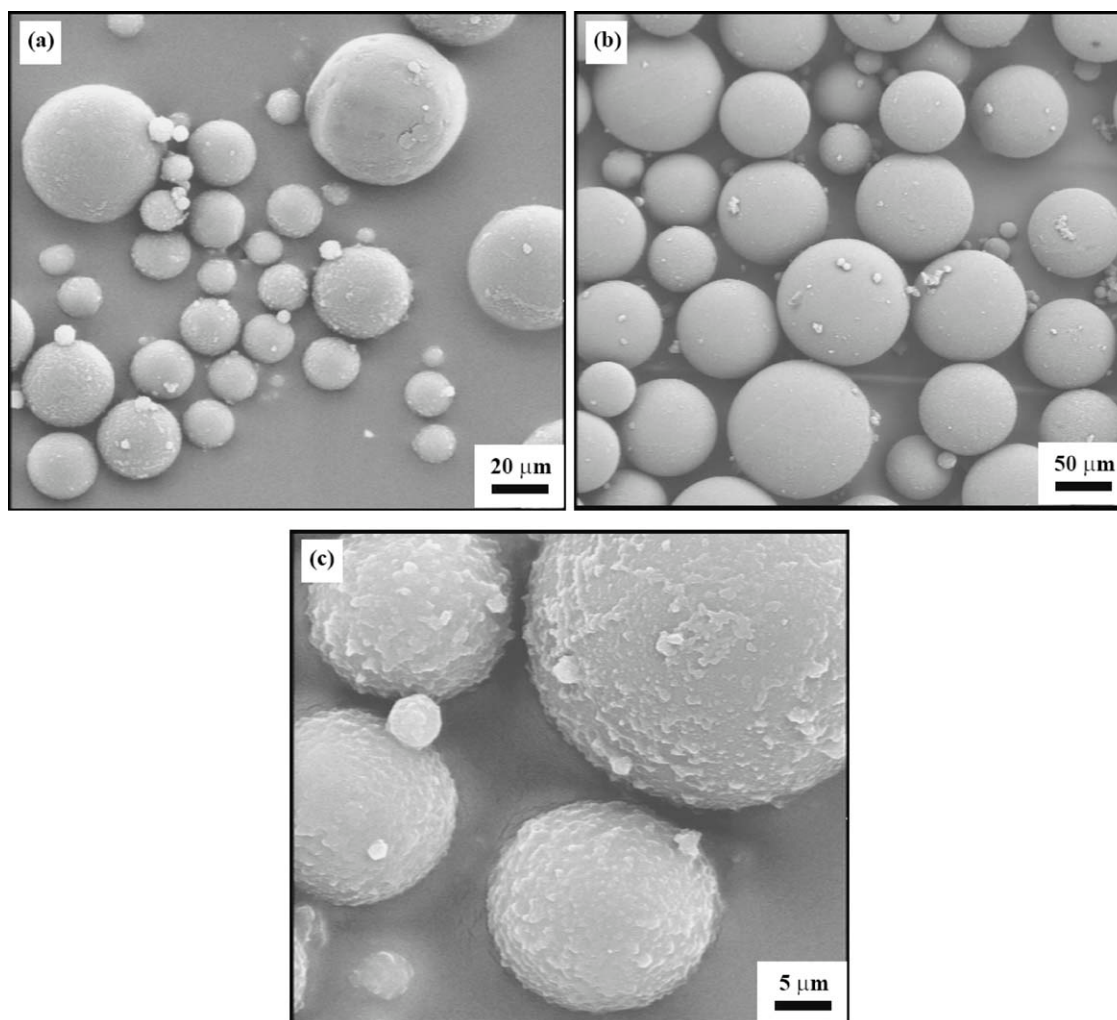
Figure 3 SEM microphotographs of the shape of microparticles of the experiments 12 and 18 (a and b, respectively) and a detail of the surface of some microparticles of the experiment 12 (c).

they are probably attached by electrostatic forces. In the case of experiment 12, Figure 3(c) shows some irregularities on the surface of the microparticles that are not appreciable either by light microscopy or at lower magnification [Fig. 3(a)]. These small surface irregularities were probably produced by abundant successive collisions between particles of very different sizes in advanced stages of the reaction, in which coalescence did not occur; instead, transient superficial fusions followed by new separations would have occurred.

Particle size distribution

The particle size distributions (PSDs), determined by laser diffraction, of some of the experiments can be observed in Figure 4, which depicts the relative volume frequency of each microparticle size. The PSDs curves show that the particle size of the microparticles obtained is generally smaller than 100 μm, as stated previously, which is a lower

mean size than that reported by other authors who used TCP as a suspension agent.[43–45] From the PSD curves, the values of d_{50} and of span can be calculated, and they are given in Tables III and VI. In general, the PSD of the microparticles obtained are bimodal. This is very usual in immiscible liquid–liquid systems when the value of the dispersed phase concentration is over 15% vol[26,46,47] and when the coalescence is negligible owing to the use of a sufficiently high concentration of surface-active agents.[48] Likewise, bimodality has been reported in the case of suspension polymerization.[17] In fact, the existence of microparticles with a mean size of around 1 μm, those of the secondary peak, is a specific feature of suspension polymerization, and this type of particle could be formed through two different mechanisms: (a) as a result of an erosive breakage, involving the removal of a number of small droplets from a larger one; (b) particle formation via dispersion and/or emulsion polymerization mechanisms.[49]
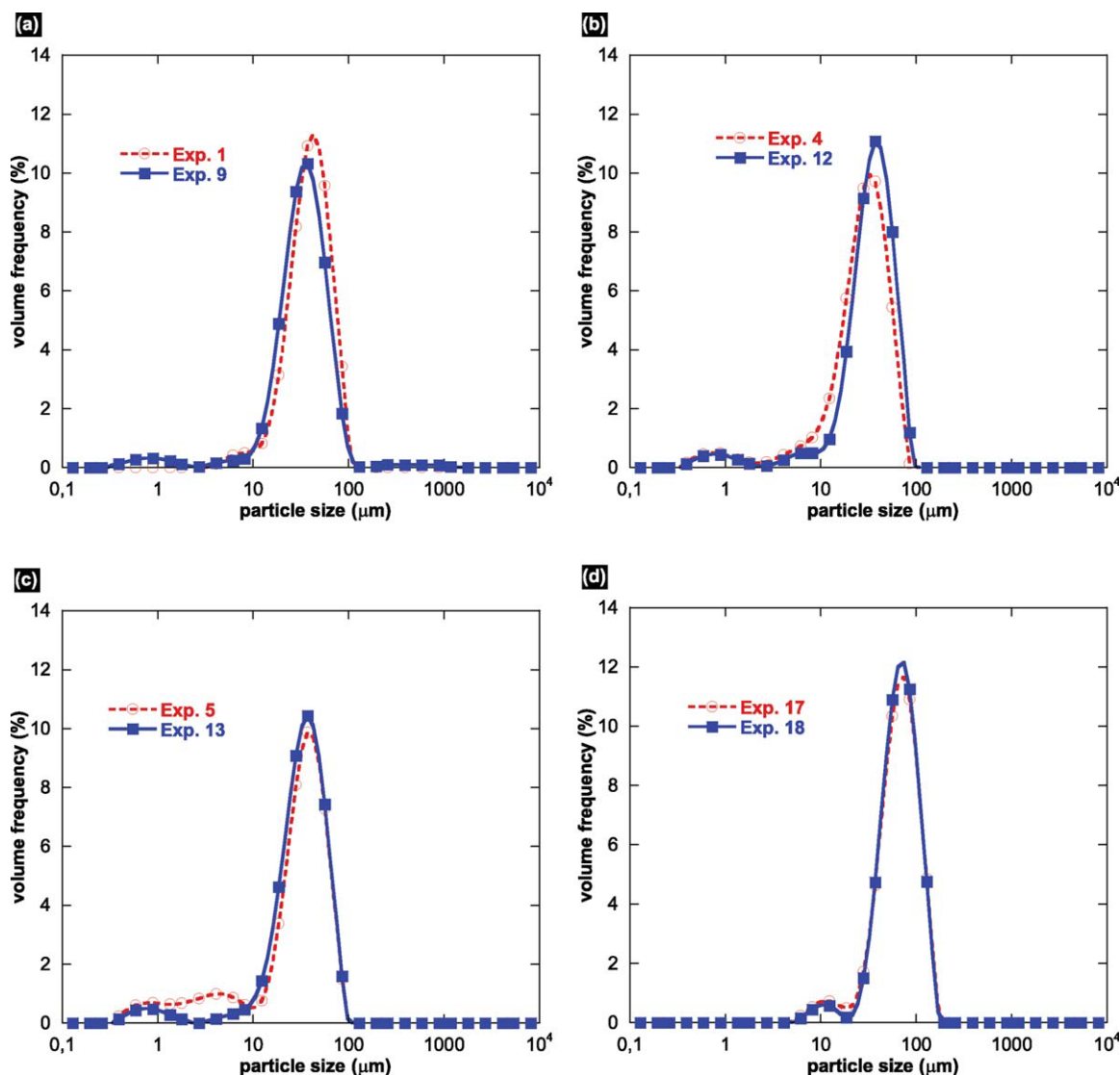
Figure 4 PSD of experiments: (a) 1 and its replicate; (b) 4 and its replicate; (c) 5 and its replicate; (d) 17 and its replicate. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Response analyses

Quality response analysis: Agglomeration and sphericity

According to Table III, the values of the indices of agglomeration and sphericity were over 0.83 for all the experiments of the factorial design, and the variation between the indices of different experiments was very small, indicating the high quality of the microparticles as regards these two properties. As a consequence of the narrow range in which these indices are located (Fig. 5), analysis of the effects of the geometric factors on the agglomeration and sphericity responses revealed that none of the geometric factors had a statistically significant influence on these responses.[41] In other words, owing to the high quality of the microparticles in regard to these characteristics for all the experiments, it is not possi-

ble to distinguish between the variability in the value of these responses due to the influence of the factors and that due to the experimental error. Furthermore, the agglomeration and sphericity indices of experiments 17–22 (see section "Additional Experiments") were also over 0.83 (they are not shown in Table VI) strengthen the idea that the quality of the microparticles obtained with regard to these properties was ensured throughout the range of this research. Therefore, it may be concluded that within the range of variation of the levels of the factors studied, no interaction occurs between the factors associated with the synthesis conditions and the factors related to the geometry of the experimental device. This being so, it may be assumed that the liquid–liquid dispersion remained stabilized throughout the polymerization process and that, consequently, the final size of the solid polymeric
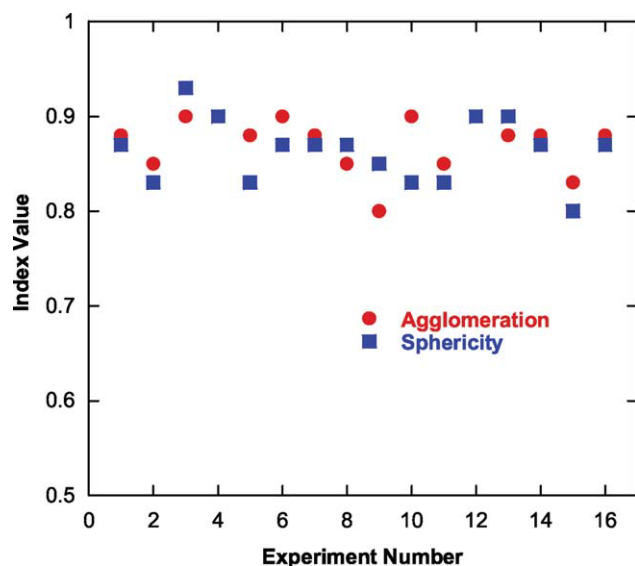
Figure 5 Plot of the values of agglomeration and sphericity indices versus the experiment number. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

microparticles was similar to the size of the liquid monomeric droplets formed at the beginning of the process.

Breadth of PSD analysis

The breadth of PSD was quantified through the determination of the span of these curves using eq. (3). The results are given in Table III for the first set of experiments. According to Table III, most of the span data show values in the range between 1.15 and 1.55, which, being lower than 2, allows the PSDs to be considered narrow.[50] Other authors have reported PSDs of microparticles obtained by suspension polymerization techniques that are not as narrow as those reported here and also with an average size larger than in this work.[32,51–53] Moreover, because those works did not provide any images of the product, it is not possible to know whether the PSDs of their polymeric product were reflecting individual microparticles or clusters of microparticles. Nevertheless, statistical analysis of the effect of the geometric factors of the experimental device on the span response revealed that none of these effects was statistically significant.[41] To explain the lack of statistically significant sources of variation in the span response, it must be taken into account that the PSD curves were based on the volume of microparticles measured throughout the microparticle size range obtained, and the span response was the ratio given by eq. (3). Thus, it must be considered that microparticles with a size smaller than 10 μm will have a strong influence on the percentile 10, despite their low volume, and that this region of distribution

is the least reproducible one, as seen in Figure 4. These facts mask the effects of the geometric factors on the span response, because the random experimental error proved to be proportionally high. Some authors, in attempts to evaluate the characteristics of PSD, have rejected the use of the very extreme points of the distributions because of their low reproducibility.[47] In other cases, these small microparticles are not shown.[32] Therefore, it may be concluded that the values of the span response showed random behavior as regards the variations in the magnitude of the geometric factors, probably because the PSDs obtained were very narrow and also because of the low reproducibility of the results of the experiments with respect to the microparticles with a strong influence on the percentile 10.

Mean size (d_{50}) analysis

After concluding from the analysis of the values of the agglomeration and sphericity indices that dispersion was stabilized throughout the suspension polymerization process, the effect of the geometric factors on the d_{50} response was studied by applying the Yates algorithm[31] to the results of the set of experiments given in Table III. The results of this analysis are summarized in Table IV and indicate that the effect of the *Stirrer diameter* (*D*) factor is the most important one in this response, followed in importance by the effect of the *Polymerization mixture volume* (*TH*) factor. Figure 6 depicts the variation in the response value when the factor changes from the low level to the high level. Thus, the factors with the highest slopes are those exerting the greatest effect, while the lowest slopes correspond to the smallest effects. Accordingly, the effect of the *D* factor is the most important and is negative; that is, the lowest values of d_{50} are upon by using the high level of this factor. In contrast, the effect of the *TH* factor is positive; that is, the lower the level of the *TH* factor, the lower the d_{50}. These results can be explained by assuming that droplet breakage occurs near the impeller and droplet coalescence in the circulation region.[54,55] This is because a larger diameter of the stirrer would expand the volume in which the

TABLE IV
Effect of the Factors and of the Interactions on d_{50}

Factor or interaction	Term	Effect
Polymerization mixture volume (Pmv.)	*TH*	8.71
Stirrer diameter (diam.)	*D*	−12.26
Width of stirrer blades (width)	*W*	2.03
Pmv. diam.	*TH·D*	−1.56
Pmv. width	*TH·W*	0.62
Diam. width	*D·W*	0.75
Pmv. diam. width	*TH·D·W*	−4.14
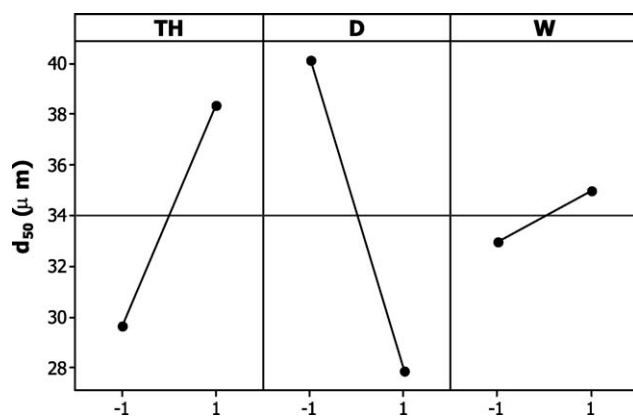
Figure 6 Plot of the effects of each factor on d_{50}.

TABLE V
ANOVA Applied to the Analysis of the Effects of the Factors on the d_{50} Response

Source of variation	Sum of squares	Degree of freedom	Mean of squares	$F_0{}^a$	P-value
TH	303.46	1	303.46	9.16	0.02
D	601.48	1	601.48	18.15	<0.01
W	16.56	1	16.56	0.50	0.50
$TH \cdot D$	9.67	1	9.67	0.29	0.60
$TH \cdot W$	1.55	1	1.55	0.05	0.83
$D \cdot W$	2.25	1	2.25	0.07	0.80
$TH \cdot D \cdot W$	68.81	1	68.81	2.08	0.19
Error	265.12	8	33.14	–	–
Total	1268.90	–	–	–	–

^{a} $F_{0.05,1,8} = 5.32$.

turbulences of the fluid surrounding the droplets of monomer are capable of producing pressure fluctuations strong enough to break the droplets and thereby reduce their average size. In contrast, by increasing the volume of the polymerization mixture, using the high level of the TH factor, there is a larger volume in which the turbulences generated by the stirrer are less intense, and, consequently, the equilibrium between the rates of break-up and coalescence moves toward the formation of larger microparticles. After the effects of the factors had been calculated, ANOVA applied to the experimental d_{50} results allowed us to know which factors had a statistically significant effect on this response. The results of the ANOVA, summarized in Table V, give the values of F statistics and their corresponding P-values for each source of variation studied (factors and their interactions). From the values calculated for the F statistics, it may be concluded that within the range investigated, the factors with a significant influence on the d_{50} are TH and D, because the values of their F statistics are higher than the tabulated value ($F_{0.05,1,8} = 5.32$, where 0.05 is the level of significance, 1 is the degree of freedom of the source of variation, and 8 refers to the degrees of freedom of the error).

Additional experiments. Having found from this first set of experiments that only the D and TH factors had a significant effect on the d_{50} response, it was decided to perform a new set of experiments (experiments 17–22), summarized in Table VI, with the multiple aim of verifying the nonsignificance of the effect of the W factor, determining the individual effect of the variables included in the TH factor, and obtaining a dimensionless model capable of allowing one the design of the experimental device, using dimensionless variables, to obtain a desirable value of the polymeric particle size. The dimensionless model was determined via the theoretical development given in Appendix A and is represented by eq. (A.9). Consequently, the experimental variables

(Table VI) of the new study were those included in this model.

Correlation between the mean size of the PSDs and the geometric factors. The model given by eq. (A.9) (Appendix A) was first transformed by using logarithms in the equation:

$$\mathrm{Ln}\left(\frac{d_{50}}{D}\right) = \mathrm{Ln}(C_2) + a \cdot \mathrm{Ln}\left(\frac{T}{D}\right) + b \cdot \mathrm{Ln}\left(\frac{H}{D}\right)$$
$$+ c \cdot \mathrm{Ln}\left(\frac{W}{D}\right) + e \cdot \mathrm{Ln}(D) \quad (4)$$

In a first attempt, eq. (4) was fitted to the experimental data to calculate the value of its parameters by using linear regression techniques, and the model given by eq. (5) was obtained:

$$\left(\frac{d_{50}}{D}\right)' = 0.037 \cdot \left(\frac{T}{D}\right)^{0.21} \cdot \left(\frac{H}{D}\right)^{0.34} \cdot \left(\frac{W}{D}\right)^{-0.02} \cdot D^{-2.20}$$
$$(5)$$

where $(d_{50}/D)'$ represents the value of the estimated ratio between the mean size of PSD and the stirrer diameter.

The fitting of the model to the (d_{50}/D) data was checked by applying ANOVA to the regression equation. The results of ANOVA, given in Table VII,

TABLE VI
Additional Experiments: Levels of the Dimensionless Geometrical Factors and Response Values

Experiment	Factor levels				Response d_{50}/D (μm/cm)
	D (cm)	T/D	H/D	W/D	
17	3.5	2	1.37	0.2	20.32
18	3.5	2	1.37	0.2	18.86
19	7.5	1.23	1.1	0.09	3.38
20	4.6	2.01	0.81	0.15	7.26
21	5.8	1.21	1.88	0.12	5.75
22	5.8	1.21	1.88	0.19	4.99

TABLE VII
ANOVA Applied to Eq. (5)

Source of variation	Sum of squares	Degree of freedom	Mean of squares	F_0	P-value
Regression[a]	4.49	4	1.12	45.43	<0.01
Residual error	0.42	17	0.02	–	–
Lack of fit	0.22	8	0.03	1.24	0.38
Pure error	0.20	9	0.02	–	–
Total	4.91	21	–	–	–

[a] $R^2 = 0.914$; $R^2_{Adj} = 0.894$.

TABLE IX
ANOVA Applied to Eq. (6)

Source of variation	Sum of squares	Degree of freedom	Mean of squares	F_0	P-value
Regression[a]	4.48	2	2.23	92.11	<0.01
Residual error	0.44	19	0.02	–	–
Lack of fit	0.13	5	0.03	1.35	0.30
Pure error	0.31	14	0.02	–	–
Total	4.91	21	–	–	–

[a] $R^2 = 0.911$; $R^2_{Adj} = 0.902$.

reveal that at least one of the regression variables contributed significantly to this model, because the P-value for the F-statistic of the regression was close to zero. In addition, the test of lack of fit indicated that this model was adequate to explain the experimental data, because the F statistic of this test was lower than the tabulated value ($F_{0.05,8,9} = 3.23$, where 0.05 is the level of significance, 8 represents the degree of freedom of the lack of fit, obtained by the difference between the degree of freedom of the residual error and that of the pure error, and 9 reflects the degree of freedom of the pure error, provided by the number of replicate experiments).

However, the difference between the values of R^2 and the adjusted R^2 statistic, R^2_{Adj}, suggests that nonsignificant terms could be included in eq. (5). Thus, to determine which regression variables had a statistically significant coefficient, a test of the significance of the individual regression coefficients was performed. The findings of this test are summarized in Table VIII.

The regression coefficients are statistically significant, with a level of significance of 0.05 when the absolute values of their t statistics are higher than $t_{0.025;17} = 2.11$, where 0.025 is the half-value of the level of significance and 17 represents the degrees of freedom of the residual error. Therefore, because the t statistics for the regression coefficients of (T/D) and (W/D) are smaller than 2.11, these regression variables were eliminated from eq. (5), and the experimental data were subjected again to multiple linear regression analysis, affording the following simplified model:

TABLE VIII
Statistical Significance of the Regression Coefficients of the Model Given by Eq. (5)

Predictor	t	P-value
Constant	7.01	<0.01
D	6.92	<0.01
T/D	0.76	0.46
H/D	2.66	0.02
W/D	0.12	0.91

$$\left(\frac{d_{50}}{D}\right)' = 0.029 \cdot \left(\frac{H}{D}\right)^{0.38} \cdot D^{-2.36} \qquad (6)$$

Also, to determine the significance of the regression, ANOVA was applied to this new model. The results, summarized in Table IX, include the values of the F-statistics and their corresponding P-values. The P-value for the F-statistic of the regression was lower than 0.01, indicating that at least one of the two regression variables contributed significantly to the reduced model provided by eq. (6). Furthermore, the coefficient of multiple determination, R^2, is relatively close to one, meaning that the model fits the experimental data well. In addition, the R^2_{Adj} is close to R^2, which confirms that nonsignificant terms have not been included in the model. With regard to the test for the lack of fit, because the F statistic calculated does not exceed the tabulated value ($F_{0.05,5,14} = 2.96$), it can be said that the reduced model given by eq. (6) fits the experimental data well and that this model can be used to predict (d_{50}/D) at any value of the D and (H/D) factors within the region studied. The significance of the individual regression coefficients was also tested, and, again, we observed that all these coefficients were statistically significant.

In this case, the good agreement between the experimental data and the estimated values of the responses (expressed by a multiple determination coefficient, R^2, relatively close to one) indicates that the correlation obtained for unreactive immiscible liquid–liquid systems can be used for reactive systems. This is only possible in the cases in which the experimental conditions used have been rendered appropriate for the stabilization of the dispersion throughout the polymerization process, this implying that the size of the initial liquid droplets is similar to that of the final polymeric solid microparticles. Consequently, the result obtained would support the idea that the experimental conditions used were suitable for the study of the quantitative effects, on the final polymeric microbead size, of the geometric factors of the experimental device that have a strong influence on the initial monomeric droplet. Thus, it may be concluded that under appropriate synthesis
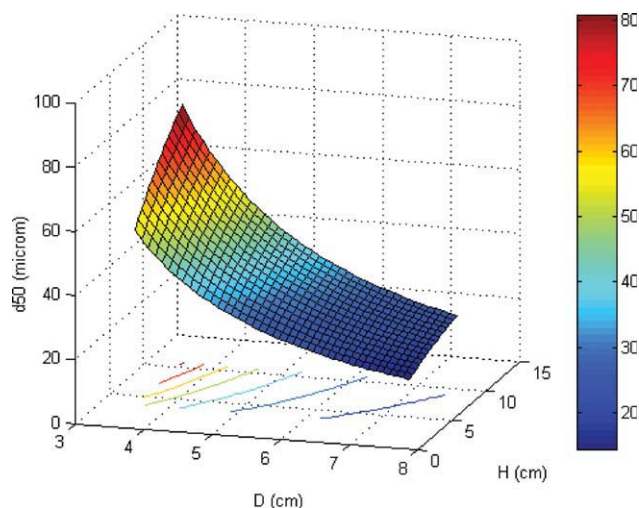
Figure 7 Surface and contour plots of d_{50}, showing the dependence of d_{50} on the significant geometrical factors of the experimental device, according to the model represented by eq. (7). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

conditions, eq. (6) could be used to design the experimental device to be used in suspension polymerization to obtain a specific microparticle mean size. Moreover, to clarify the effect of the variables included in eq. (6) on the d_{50}, it can be reorganized as follows:

$$d'_{50} = 0.029 \cdot H^{0.38} \cdot D^{-1.74} \tag{7}$$

where d'_{50} is the estimated value of d_{50}.

The final model given by eq. (7) indicates that the value of the mean size of PSD (d_{50}) decreases upon using larger stirrer diameters (D) and lower depths of liquid inside the reactor (H) during the suspension polymerization process. These effects can be clearly perceived in the surface plot generated by eq. (7), depicted in Figure 7.

With regard to the effect of the H factor, from the statistical analysis of the effect of the factors, it was found that the TH factor had a significant influence (Table V) on the d_{50} response. However, because eq. (7) shows that the tank diameter (T) does not have a significant influence on the d_{50} response, it may be concluded that the influence of the TH factor on polymeric particle size is mainly due to the variable H. These findings support the idea that the break-up of the droplets mainly occurs in the impeller region, such that an enlargement of the diameter of the stirrer blades contributes to the formation of smaller droplets, because any increase in the break-up rate moves the equilibrium between the rates of break-up and coalescence toward a decrease in the droplet diameter achieved. By contrast, any increase in the depth of the liquid inside the reactor expands the size of the region of circulation and the break-up

and coalescence rates decrease, leading to an increase of the equilibrium size of the droplets.

CONCLUSIONS

Gel-type poly(styrene-*co*-divinylbenzene) microparticles were synthesized with the suspension polymerization technique. By using a set of suitable synthesis conditions, with which it was possible to obtain polymeric microbeads with optimum values of their morphological characteristics, a study was made of the effect of the geometric factors of the experimental device on (a) the morphological characteristics of the microparticles, designated as *agglomeration* and *sphericity indices* and (b) the *mean* (d_{50}) and *breadth* (span) of the PSD. The research was first planned through a factorial design of experiments, and, upon analyzing the results obtained for the agglomeration and sphericity indices, it may concluded that the stability of dispersion was achieved in all the experiments despite changing the magnitudes of the geometric factors and keeping the values of the synthesis conditions constant. In the case of the span response, the PSDs obtained were very narrow, although the low reproducibility of the particle size, in the case of the smallest microbeads, did not allow us to determine the effect of the geometric factors on this response. For the d_{50} response, it was seen that the *Stirrer diameter* and *Polymerization mixture volume* factors affect the values of this response, and it was found that the higher the *Stirrer diameter* and the lower the *Polymerization mixture volume*, the lower the mean value of the PSD of the polymeric product. In addition, after the analysis of the results of the first set of experiments, it was decided to expand the experimentation region to fit a dimensionless model to the experimental data by using multiple linear regression analysis. Under the operation conditions used here, the dimensionless model obtained indicates that, once the stabilization of dispersion has been achieved by using a suitable set of synthesis conditions, the final polymeric microparticle size decreases by using a larger stirrer diameter and lower liquid depth inside the reactor. Therefore, it can be stated that the effect found for the factor *Polymerization mixture volume* was mainly due to the liquid depth inside the reactor. These findings are consistent with the action of the stirring in immiscible liquid–liquid systems, in which droplet size is decreased when the impeller zone, where the break-up of the dispersed droplets are more intense than the coalescence, is expanded, while the opposite occurs in the circulation zone. Furthermore, the model developed permits the design of experiments aimed at the preparation of polymeric particles smaller than 100 μm and with a median of PSD smaller than 50 μm.

NOMENCLATURE

a	empirical coefficient, equal to $-0.4\ a'$ [eq. (A.9)]
a'	empirical coefficient [eq. (A.4)]
b	empirical coefficient, equal to $-0.4\ b'$ [eq. (A.9)]
b'	empirical coefficient [eq. (A.4)]
BPO	benzoyl peroxide
c	empirical coefficient, equal to $-0.4\ c'$ [eq. (A.9)]
c'	empirical coefficient [eq. (A.4)]
C_1	empirical constant [eq. (A.1)]
C'_1	empirical constant [eq. (A.2)]
C''_1	empirical constant [eq. (A.8), $cm^{1.8}$]
C_2	empirical constant [eq. (A.9), cm^{-e}]
D	stirrer diameter (cm)
d_{90}	diameter for which 90% of the particles in the sample are smaller than that diameter, percentile 90 (μm)
d_{50}	mean diameter of the PSD (μm or cm).
d_{10}	diameter for which 10% of the particles in the sample are smaller than that diameter, percentile 10 (μm)
d_{32}	Sauter mean diameter (cm)
DVB	divinylbenzene
d'_{50}	predicted value of d_{50} (cm)
$(d_{50}/D)'$	predicted value of the ratio of d_{50} and D
e	empirical coefficient, equal to $(-0.4)\cdot(2\ e' + f) - 1.8$, [eq. (A.9)]
e'	empirical coefficient [eq. (A.4)]
f'	empirical coefficient [eq. (A.4)]
F	Fisher statistic
F_0	calculated Fisher statistic
Fr	Froude number
g	gravitational acceleration (cm s^{-2})
H	liquid depth inside the reactor (cm)
K	empirical constant [eq. (A.4)]
K'	empirical constant [eq. (A.7)] [$cm^{-(2e'+f')}$]
N	stirring rate (rpm or rps)
N_P	power number
$N^{\circ}{}_x$	number of portions with the x feature [eqs. (1) and (2)]
$N^{\circ}{}_{Features}$	number of features related to the agglomeration and sphericity indices [eqs. (1) and (2)]
$N^{\circ}{}_{Portions}$	number of portions scrutinized under the optical microscope [eqs. (1) and (2)]
P	power input by the impeller (g cm^2 s^{-3})
PSD	particle size distribution
r_1	constant that includes the kinematic viscosity and the stirring rate (cm^{-2})
r_2	constant that includes the squared stirring rate and the acceleration due to gravity (cm^{-1})
R^2	coefficient of multiple determination
R^2_{Adj}	adjusted coefficient of multiple determination
Re	impeller Reynolds number
SDS	sodium dodecyl sulfate
span	response span, quantification of the breadth of the PSD [Eq. (3)]
St	styrene
t	Student's statistic
T	reactor diameter (cm)
TCP	tricalcium phosphate
TH	polymerization mixture volume
W	width of stirrer blades (cm)

Greek letters

ν	kinematic viscosity (cm^2 s^{-1})
ρ	density (g cm^{-3})
σ	interfacial tension between the two phases (g s^{-2})

APPENDIX A: MODEL DEVELOPMENT

A basic relationship to determine the Sauter mean diameter, d_{32}, in a dispersion of two immiscible liquids with negligible coalescence, low viscosity of the dispersed phase, and stirred by a Rushton turbine in a baffled reactor was given by Shinnar and Church[38] and is shown in eq. (A.1):

$$\frac{d_{32}}{D} = C_1 \left(\frac{\rho \cdot N^2 \cdot D^3}{\sigma} \right)^{-0,6} \tag{A.1}$$

where C_1 is an empirical constant that depends on the tank geometry and on the type and geometry of the stirrer; ρ is the density (it is usual to employ the density of the continuous phase); σ is the interfacial tension between the two phases; N is the stirring rate, and D is the stirrer diameter. In practice, the value of d_{32} is similar to that of the mean diameter of the PSD measured by volume, d_{50}, and therefore these two values can be interchangeable.[36]

The mean size of dispersed droplets has been predicted by eq. (A.1) for a number of liquid–liquid systems, with a wide range of liquid properties.[56,57] However, although it is clear that the characteristics of the circulation of the fluids do have an effect on mean droplet size, this equation does not include any parameter related to this factor. Therefore, McManamey[58] modified the correlation given by

eq. (A.1) to include the effect of this factor on mean droplet diameter by assuming that the power input due to stirring is dissipated in the impeller-swept volume, introducing the correlation given by eq. (A.2):

$$\frac{d_{50}}{D} = C'_1 \cdot N_p^{-0.4} \cdot \left(\frac{\rho \cdot N^2 \cdot D^3}{\sigma}\right)^{-0,6} \quad \text{(A.2)}$$

where N_P is the power number and C'_1 is an empirical constant. Because this relationship was initially proposed considering that the dissipation of the stirring energy occurs in the impeller zone, the power number must be calculated assuming the effect of the environment in which the impeller is functioning.[35] Thus, this equation should be applied considering that the volume through which the energy is dissipated is the whole volume of the stirred liquid; that is, the geometry of the stirred tank that shapes the liquid volume should be included in this equation.

The power number, N_P (also known as the Newton number), is a dimensionless number relating the resistance force to the inertia force, and it provides a measure of the power requirements for the operation of an impeller. It is defined as

$$N_p = \frac{P}{\rho \cdot N^3 \cdot D^5} \quad \text{(A.3)}$$

where P is the power input by the impeller.

Rushton et al.[35] studied the effect of stirring on stirred tanks and, by dimensional analysis, found a correlation for N_P as a function of the geometric magnitudes of the stirrer, the environment that surrounded it, the kinematic and dynamic characteristics of the liquid movement, and the properties of the fluid. This relationship, in which the only geometric variables of the experimental device are the tank diameter, the depth of liquid inside the reactor, and the width of stirrer blades, can be written as in eq. (A.4):

$$N_p = K \cdot \left(\frac{T}{D}\right)^{a'} \cdot \left(\frac{H}{D}\right)^{b'} \cdot \left(\frac{W}{D}\right)^{c'} \cdot Re^{e'} \cdot Fr^{f'} \quad \text{(A.4)}$$

where K is an empirical constant, T is the tank diameter, H is the liquid depth inside the reactor, W is the width of stirrer blades, D is the stirrer diameter, Re is the impeller Reynolds number ($= (D^2 N)/\nu$, ν being the kinematic viscosity); Fr is the Froude number ($= (DN^2)/g$, g being the gravitational acceleration), and a', b', c', e', and f' are empirical coefficients. The Froude number must be included, because baffles inside the experimental device were not used in this work, and therefore the ratio between the inertia

and gravitational forces could have an important effect on the stirring regime.[35]

Taking into account the definitions of the Re and Fr numbers, when carrying out experiments with the same substances, at the same proportions, and with identical stirring rates in all the experiments, they can be written as

$$Re = r_1 \cdot D^2 \quad \text{(A.5)}$$
$$Fr = r_2 \cdot D \quad \text{(A.6)}$$

where r_1 represents a constant that includes the kinematic viscosity and the stirring rate and r_2 comprises the squared stirring rate and the acceleration due to gravity. This means that in these cases, the variation in the dimensionless Froude and Reynolds numbers from one experiment to another is exclusively due to the stirring diameter, because the remaining variables, on which these two parameters depend, remain unmodified.

Thus, eq. (A.4) can be transformed into eq. (A.7):

$$N_p = K' \cdot \left(\frac{T}{D}\right)^{a'} \cdot \left(\frac{H}{D}\right)^{b'} \cdot \left(\frac{W}{D}\right)^{e'} \cdot D^{(2e'+f)} \quad \text{(A.7)}$$

where $K' = K \cdot r_1^{e'} \cdot r_2^{f''} = K \cdot (N/\nu)^{e'} \cdot (N^2/g)^{f''}$.

Moreover, when the substances were used, their proportions and the stirring rate are constant for all the experiments, and eq. (A.2) can be rewritten as follows:

$$\frac{d_{50}}{D} = C'_1 \cdot N_p^{-0,4} \cdot \left(\frac{\rho \cdot N^2 \cdot D^3}{\sigma}\right)^{-0,6} = C''_1 N_p^{-0,4} \cdot D^{-1,8} \quad \text{(A.8)}$$

where $C''_1 = C'_1 \cdot (\rho \cdot N^2/\sigma)^{-0,6}$

Therefore, by introducing eq. (A.7) into eq. (A.8), we obtain eq. (A.9):

$$\frac{d_{50}}{D} = C_2 \cdot \left(\frac{T}{D}\right)^a \cdot \left(\frac{H}{D}\right)^b \cdot \left(\frac{W}{D}\right)^c \cdot D^e \quad \text{(A.9)}$$

where C_2 ($= C''_1 \cdot K'^{-0,4}$) is an empirical constant that involves all the invariable geometric factors of the experimental device, the properties of the substance used, and the synthesis conditions held constant, and a ($= -0.4\, a'$), b ($= -0.4\, b'$), c ($= -0.4\, c'$), and e [$= (-0.4)\cdot(2e' + f)-1.8$] are the new empirical coefficients.

Equation (A.9) establishes a quantitative relationship between the values of the mean of the particle size distribution and the geometric magnitudes of the experimental device. Taking into account that Eq. (A.9) is deduced from correlations for unreactive immiscible liquid–liquid systems, it must be

considered that this correlation would be useful for predicting the values of the final polymeric particle size only in the case in which the stabilization of the dispersion is attained throughout the suspension polymerization process, because only in this case will the final size of the particles be similar to that of the monomeric droplets formed during the first stage of the polymerization process, in which only an immiscible liquid–liquid system is stirred.[14,32] This implies that in spite of the variation in viscosity and degree of stickiness of the organic phase during the progression of the polymerization reaction, the coalescence of monomeric droplets and the agglomeration of polymeric microparticles should not affect the final size of the polystyrene-based microparticles, owing to the efficiency of the protective mechanisms. Therefore, the applicability of Eq. (A.9) to the results of the suspension polymerization would demonstrate the possibility of expanding the use of the correlations obtained for unreactive immiscible liquid–liquid systems to others in which a chemical reaction occurs, and hence the possibility that these kinds of equation could be used in the design of equipment in which reactive processes are to be carried out.

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