



Synthesis and characterization of polyurethane and poly(ether urethane) nanocapsules using a new technique of interfacial polycondensation combined to spontaneous emulsification

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Received 14 February 2003; received in revised form 25 July 2003; accepted 1 September 2003

Abstract

Polyurethane polymers and poly(ether urethane) copolymers were chosen as drug carriers for α -tocopherol. This active ingredient is widely used as a strong antioxidant in many medical and cosmetic applications, but is rapidly degraded, because of its light, heat and oxygen sensitivity. Polyurethane and poly(ether urethane)-based nanocapsules were synthesized by interfacial reaction between two monomers. Interfacial polycondensation combined with spontaneous emulsification is a new technique for nanoparticles formation. Nanocapsules were characterized by studying particle size (150–500 nm), pH, yield of encapsulation and morphologies. Polyurethanes (PUR) were obtained from the condensation of diisocyanate (isophorone diisocyanate: IPDI) and polyol: 1,2-ethanediol (EG), 1,4-butanediol (BD), 1,6-hexanediol (HD). Poly(ether urethane) copolymers were obtained by replacing diols by polyethylene glycol oligomers (PEG) M_w 200, 300, 400 and 600. Molecular weights of di- and polyols have a considerable influence on nanocapsules characteristics cited above. The increase of molecular weight of polyols tends to increase the mean size of nanocapsules from (232 ± 3) nm using EG to (615 ± 39) nm using PEG 600, and led to the apparition of a population of agglomerate particles. We also noted that the yield of encapsulation increases with the increase of polyol length (from 85.6 to 92.2% w/w). Microscopic observations confirmed particle size analysis, but cannot predict the membrane structure owing to the small size of the particles.

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Keywords: Polyurethane; Poly(ether urethane); Nanocapsules; α -Tocopherol; Encapsulation; Interfacial polycondensation; Spontaneous emulsification

1. Introduction

At present, various techniques are known for preparing colloidal dispersions containing nanopar-

ticles, particularly with lipophilic core. These techniques include nanoprecipitation, salting-out and emulsification-evaporation, which involve an organic solution, as an internal phase during preparation, and an aqueous solution, containing stabilizers which will constitute the dispersing medium for the nanoparticles. These techniques involve preformed synthetic polymers such as, poly(ethylene oxide), poly(lactic

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acid), poly(lactide-co-glycolide), poly(ϵ -caprolactone) (Guinebretière, 2001), chitosan (Chandra and Rustgi, 1998).

In this paper we use a new technique of interfacial polycondensation to encapsulate ϵ -tocopherol using polyurethane and poly(ether urethane) nanocapsules. Polyurethanes are an important class of polymers that have found many applications as biomaterials due to their excellent physical properties and relatively good biocompatibility (Chen et al., 2000; Boretos and Cooper, 1967; Lan et al., 1996). Polyurethanes derive from the polycondensation of diisocyanates (hard segments with $\text{N}=\text{C}=\text{O}$ groups) and di- or polyols (soft segments with OH groups).

The polyurethanes used in this study are relatively interesting because of their widespread characteristics related to the nature of monomers (Boretos, 1980; Sharma et al., 1988; Szycher and Poirier, 1983; Yui et al., 1988 and Kohjiya et al., 1991). Especially, poly(ether urethanes) have been greatly studied due to their excellent physical properties (flexibility, T_g , degradation, etc.), resistance for infectiousness, and superior compatibility (Langer and Folkman, 1980; Kohjiya and Ikeda, 1989; Lelah et al., 1983). Poly(ether urethanes) copolymers are obtained by replacing short chain diols monomers (ethylene glycol, butanediol, hexanediol) by high molecular weight polyethylene glycols oligomers (PEG).

In the literature, polyurethanes were essentially used for microparticles preparation with an average size from 10 μm (Hong and Park, 1999) to 50–200 μm (Frère et al., 1998). In the classical interfacial polycondensation, two steps are necessary (Bouchemal et al., 2002):

- Emulsification step: O/W emulsion formation using a mechanical stirring during few minutes. Diisocyanate monomer is enclosed in the emulsion drops.
- Polymerisation steps: the second complementary monomer (di or polyols) is added to the external phase of the emulsion and the polycondensation reaction takes place at the liquid-liquid emulsion interface.

Polyurethanes encapsulation studies were exclusively limited to *microparticles* systems using the classical interfacial polycondensation. The operating parameters were optimized by studying monomer concentration (Zhang et al., 1995), reaction tempera-

ture (Frère et al., 1998), variation of the emulsifying and polymerization time (Yan et al., 1992; Zhang et al., 1995), stirring rate (Bouchemal et al., 2002), and surfactant concentration (Zhang et al., 1995).

The emulsion step is of major importance in the classical interfacial polycondensation process, as it determines the droplets size distribution and so the particles one. An important quantity of mechanical energy is maintained during few minutes to achieve the emulsification step. To perform this step and achieve a stable size distribution, mechanical energy is necessary during few minutes; there is a possibility of diisocyanate hydrolysis by reaction with water. Furthermore, the active agent could diffuse to the continuous phase while decreasing the yield of encapsulation (Frère et al., 1998).

The originality of our study resides on the use of the new interfacial polycondensation combined with spontaneous emulsification technique for polyurethane based nanocapsules synthesis. In the new interfacial polycondensation technique, spontaneous emulsification process was explored to form submicronic particles supplying low energy (magnetic stirring). It is a one-step procedure, where an organic phase composed of a water miscible solvent, diisocyanate monomer, oil and a lipophilic surfactant, is injected in an aqueous phase containing diol or polyether and the hydrophilic emulsifying agent. The water miscible solvent should diffuse to the aqueous phase, the oil precipitates as nano-droplets, and the two monomers react at the interface, forming a membrane around the nano-emulsion leading to nanocapsules. According to studies concerning classical interfacial polycondensation, the influence of some operating parameters was studied in order to optimize the polyurethane-based nanocapsules formation. We applied this technique to the encapsulation of α -tocopherol or vitamin E (VE). This active agent is widely used as an antioxidant in many medical and cosmetic applications, but is rapidly degraded, because of its light, heat and oxygen sensitivity. Thus, all of its formulation has to avoid contact with light, heat or air. Drug loaded carriers such as nanoparticles are an attractive opportunity especially when the size, the yield of encapsulation and other nanocapsules properties could be controlled.

In this paper, we evaluate the effects of soft segments length variations in the polyurethane-based

nanocapsules properties, by changing the molecular weight of polyols. The nanocapsules suspensions will be introduced in cosmetic and pharmaceutical formulations to topical administration.

2. Materials

2.1. Monomers

Ethylene glycol (ED), 1,4-butanediol (BD), 1,6-hexanediol (HD) with low molecular weight and polyethylene glycol (PEG 200, 300, 400, 425, 600) with high molecular weight as polyols, and isophorone diisocyanate (IPDI) as diisocyanate, were obtained from Sigma, France.

2.2. Solvents

Acetone and isopropanol were obtained from Sigma, France.

2.3. Active agent

α -Tocopherol was obtained from Coletica, France.

2.4. Surfactants

(Span[®] 80, Span[®] 85, Tween[®] 20, Tween[®] 80, Pluronic[®] F68) were supplied by SEPPIC, France. Lipoide[®] S75 is obtained from Lipoid GmbH Ludwigshafen, Germany.

3. Methods

3.1. Nanocapsules preparation

The methodology for obtaining nanocapsules by interfacial polycondensation combined with spontaneous emulsification presents three steps (Fig. 1):

- Preparation of the homogeneous organic solution composed of IPDI (10^{-3} mol), α -tocopherol (400 mg) and a lipophilic surfactant (86 mg Span[®] 85) in water-miscible solvent (40 ml acetone) (S_1). The homogeneous aqueous phase (S_2) is formed by water (80 ml), diol or polyether (10^{-2} mol) and hydrophilic surfactant (136 mg Tween[®] 20).

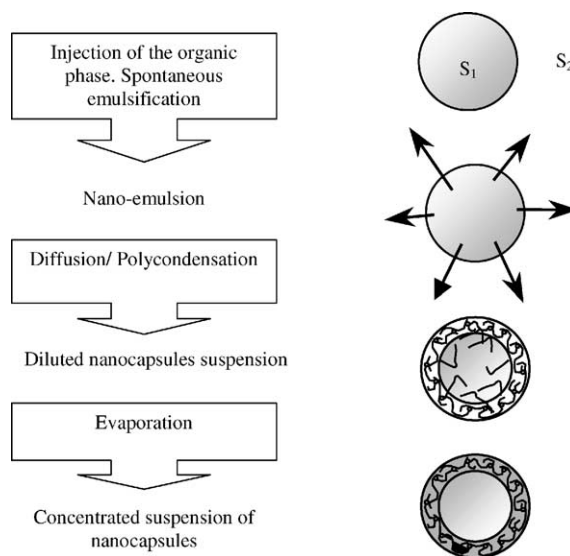


Fig. 1. Mechanism of nanocapsules preparation using the new interfacial polycondensation technique (Montasser et al., 2001).

- Injection of the organic phase in the aqueous phase under magnetic stirring: the nanocapsules precipitate instantaneously, and the primary membrane is formed immediately. The magnetic stirring is maintained during 3 h at room temperature in order to ensure the wall growth (maturation step).
- The totality of the solvent (acetone) as well as a part of the water is removed by evaporation during 45 min under reduced pressure.

3.2. Polymer characterization

The polymer structure was confirmed by using Fourier transform infra-red spectroscopy (FT-IR) and nuclear magnetic resonance spectroscopy (^1H NMR).

FT-IR spectra were obtained with a Perkin-Elmer 1600 series FT-IR spectrometer.

3.3. Nanocapsules characterization

3.3.1. Particle size and size distribution

The particle size distribution of the prepared nanocapsules were measured in an aqueous suspension by static laser light scattering on a LS 230 COULTER[®] granulometer. The LS 230 measures particle size distribution using the principle of laser diffraction. A sample placed in the fluid module is

circulated through a sample cell at constant speed. A beam of laser light shone through the cell is diffracted by particles within the sample, and the forward scattered (or diffracted) light is collected by a series of detectors. Information about particles smaller than $0.4\ \mu\text{m}$ is limited in diffraction pattern, so another technique is used. Thus, the LS 230[®] includes another measurement assembly, called polarization intensity differential scattering (PIDS). The PIDS assembly consists of an incandescent light source and polarizing filters, a PIDS sample cell and an additional seven photodiode detectors (six to measure scattered light plus one to monitor the beam strength).

To measure the particle size distribution, 0.5 ml suspension is introduced in the measure compartment (125 ml of water). The results were presented as volume fraction distribution.

3.3.2. pH

pH values of the nanocapsules aqueous suspensions were measured with a pH meter (PHM210. MeterLab[®]) by simply plunging the electrode into the nanosuspension.

3.3.3. Nanocapsules morphologies

The shape and the morphology of the produced nanoparticles were investigated by the transmission electron microscopy (TEM) Topcon[®] EM002B, 200 kV. Usually, samples are prepared by placing a drop of preparation on a collodion support on cooper grids (Malaiya and Vyas, 1988), followed by negative staining with an aqueous solution of sodium phosphotungstate (Al Khouri et al., 1986a; Rollot, 1986; Seijo et al., 1990; Al Khouri et al., 1986b), phosphotungstic acid (Fessi et al., 1989) or uranyl acetate.

3.3.4. Yield of encapsulation

Total α -tocopherol concentration (T_α) was determined after dissolution of nanoparticles in isopropanol solvent followed by 30 min on ultrasounds. Free α -tocopherol was determined after separation of loaded-nanoparticles from the aqueous medium by an ultracentrifugation technique (OptimaTM Ultracentrifuge, BEKMAN-COULTER Instruments, USA). Ultracentrifugation of $4.5 \times g$ was carried out in Beckman OptimalTM tubes (11 ml) housed in a MLA-80 rotor in an OptimaTM MAX Tabletop ultracentrifuge. All tubes were centrifuged at 45 000 rpm

for 20 min at 20°C . The yield of encapsulation (Y) was calculated as follows:

$$Y = \frac{L_\alpha}{T_\alpha} \times 100 \quad (1)$$

where L_α is the α -tocopherol concentration in loaded nanoparticles, T_α is the total concentration of α -tocopherol introduced in the preparation.

α -Tocopherol concentration in loaded nanoparticles (L_α) was obtained as followed. The suspension samples ultracentrifuged at 45,000 rpm. The supernatant containing loaded nanocapsules was isolated, we completed to $4.5 \times g$ using (Water/Tween[®] 20) mixture at 0.33%. This washing operation was reproduced two times. Then, the nanocapsules (10 mg) were digested in 20 ml of isopropanol and passed 30 min on ultrasounds. α -Tocopherol concentration was determined by HPLC analysis.

3.4. HPLC analysis

The samples were assayed using high-performance liquid chromatography (HPLC). A ChromoQuest thermoquest France SA instruments was used with a Lichrospher RP 18-e ($5\ \mu\text{m}$, $125\ \text{mm} \times 4\ \text{mm}$). The mobile phase consisted of methanol. The flow rate was 1 ml/min. A $40\text{-}\mu\text{l}$ sample size was injected. α -Tocopherol was detected using a variable wavelength UV detector at 285 nm and results were quantified through the use of the equation derived from the slope of the standard curve prepared for α -tocopherol ($r = 0.9998$) at 285 nm.

4. Results and discussion

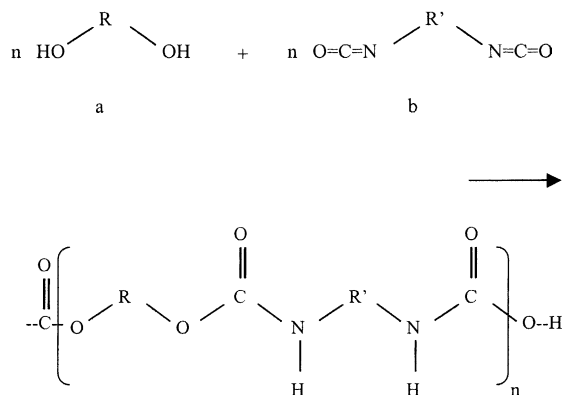
4.1. Nanocapsules characterization

4.1.1. Polycondensation reaction and polymer characterization

In the first reaction (1), isocyanate groups (b) react with hydroxyl groups of diols or polyethers (a) to form polyurethane chains. In the second reaction corresponds to $-\text{N}=\text{C}=\text{O}$ hydrolysis. Isocyanate groups react with water by diisocyanate diffusion to the aqueous phase forming an acid amic group (c), which is unstable and dissociates into a chain with amine end-group (d) and carbon dioxide (Jabbari and

Khakpour, 2000). There is other secondary reactions such as the formation of urea, biuret, allophanate, dimerisation and trimerisation reaction (Bolognisi et al., 2001).

Polymerization reaction

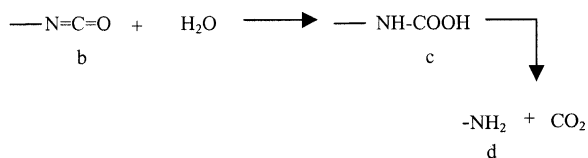


R=-(CH₂)₂ Ethylene glycol

R=(CH₂)₄ Butanediol

R=(CH₂)₆ Hexanediol

Reaction (1): Polyurethane polymer formation (Jabbari et al., 2000)



Reaction (2): Isocyanate groups react with water (Bolognisi et al., 2001)

The principle of the polyurethane film formation by interfacial polycondensation is well described in different reviews and publications always applied to the formation of microcapsules (Arshady, 1989; Morgan, 1987; Janssen and Te Nijenhuis, 1992). The mean particles size obtained by the new technique of interfacial polycondensation is less than 400 nm, a substance in the form of nanoparticles has several importance characteristics. First of all, nanoparticles present an enormous surface area, which makes such substance suitable for important pharmaceutics and cosmetics applications like topical formulations of lipophilic

encapsulated drugs for an homogeneous release. Furthermore, the increase of the surface area results on the increase of the polycondensation reaction kinetic.

The characterization of the chemical structure of the polyurethane polymer is informative for the performance of the encapsulation experiments and for the quantitative identification that the right polymer was formed.

The completion of polycondensation reaction between IPDI and polyol was confirmed by FT-IR analysis. FT-IR spectra of nanocapsules containing α -tocopherol is presented in Fig. 2. The spectrum shows absorption bands at 1740–1700 cm⁻¹ for the C=O vibration of urethane and at 1690–1650 cm⁻¹ for urethane-urea formation. The N–H vibration was observed at 3450–3300 cm⁻¹. The IR spectrum also indicates the completion of the reaction between diisocyanate and polyol by the disappearance of the NCO absorption band at 2270 cm⁻¹ and appearance of the N–H and C=O vibration at 2850 cm⁻¹, C–O–C stretching at 1107 cm⁻¹, and =C–H bending at 880–750 cm⁻¹ are also observed.

4.1.2. Particle size distribution

The size of nanocapsules is usually found to be between 100 and 500 nm and depends on several factors: the nature and the concentration of monomers and of the loaded drug, the amount of surfactants, the ratio of organic solvent to water, the concentration of oil in the organic solution (Chouinard et al., 1991) or the rate of diffusion of the organic phase into the aqueous phase.

It can be seen in Fig. 3 that the size distribution obtained with diol of low molecular weight (ethylene glycol, butanediol and hexanediol) are very similar. However, the increase in the molecular weight of polyethylene glycols from PEG 200 to PEG 600 leads to modification of the size distribution.

4.1.2.1. Poly(ether urethane) nanoparticles. Fig. 4 shows the particle size distribution of poly(ether urethane) nanoparticles with different molecular weight of PEG (*M_w* 200, 300, 400, 600). Polyethylene glycols are polymers of ethylene oxide with the generalized formula HO–(CH₂–CH₂–O)_{*n*}–H, where *n* indicates the average number of oxyethylene groups. The mean size of the prepared particles increased up: (218 ± 3), (275 ± 32), (621 ± 3) and (615 ± 39) nm, a second population of microparticles appears and becomes

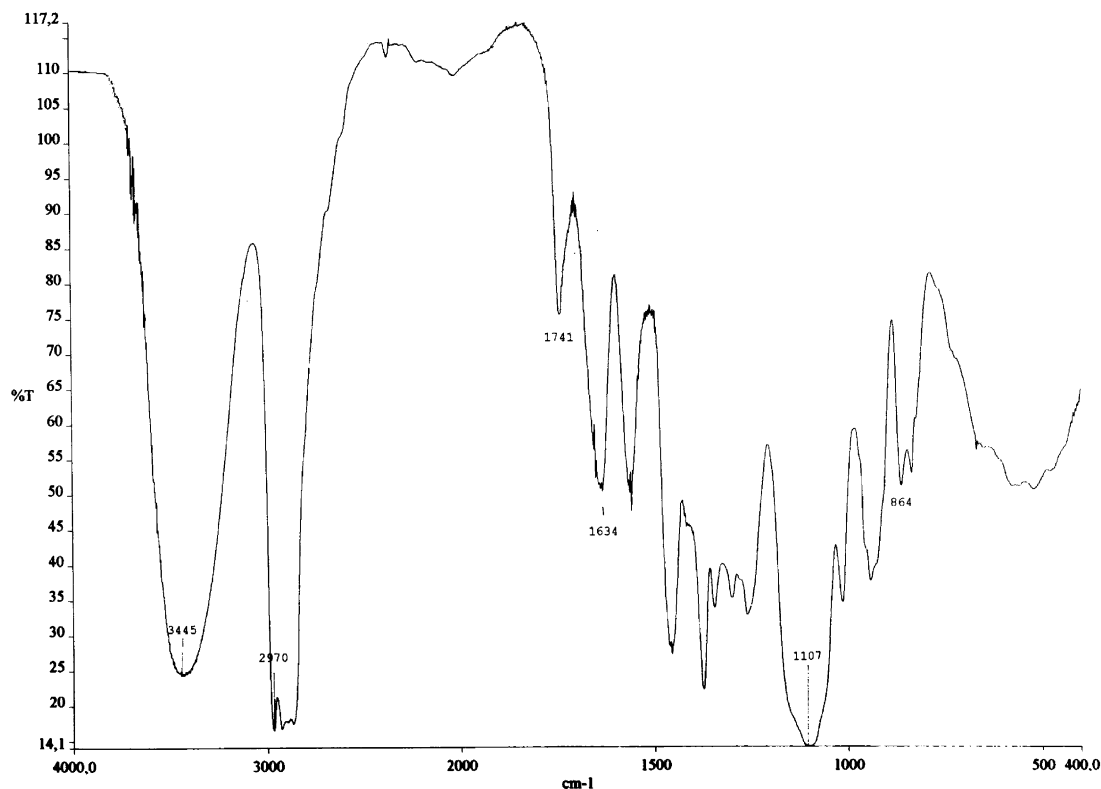


Fig. 2. FT-IR spectra of polyurethane nanocapsules.

wider with the molecular weight increase. Several assumptions could be proposed for the explanation of the apparition of this second population.

In the process of nanodroplets precipitation, globules would instantaneously be of the same small size,

but agglomeration could occur by the presence of polyethers with various molecular weights into the solution, which resulted from an increase of system viscosity (Tables 1 and 2) and larger particles are produced.

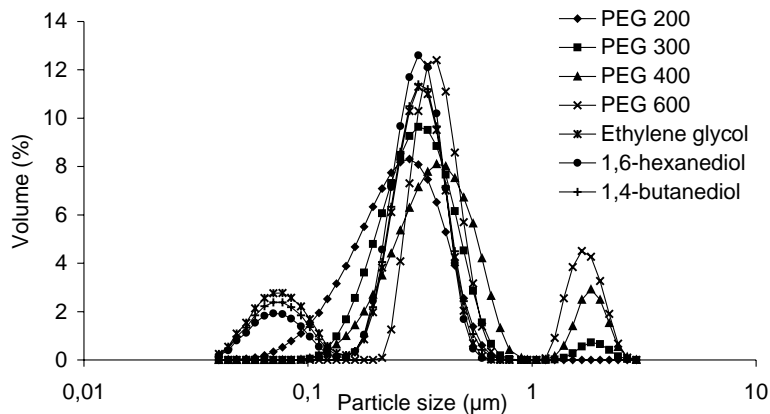


Fig. 3. Particle size distribution of polyurethanes and poly(ether urethane) based nanocapsules.

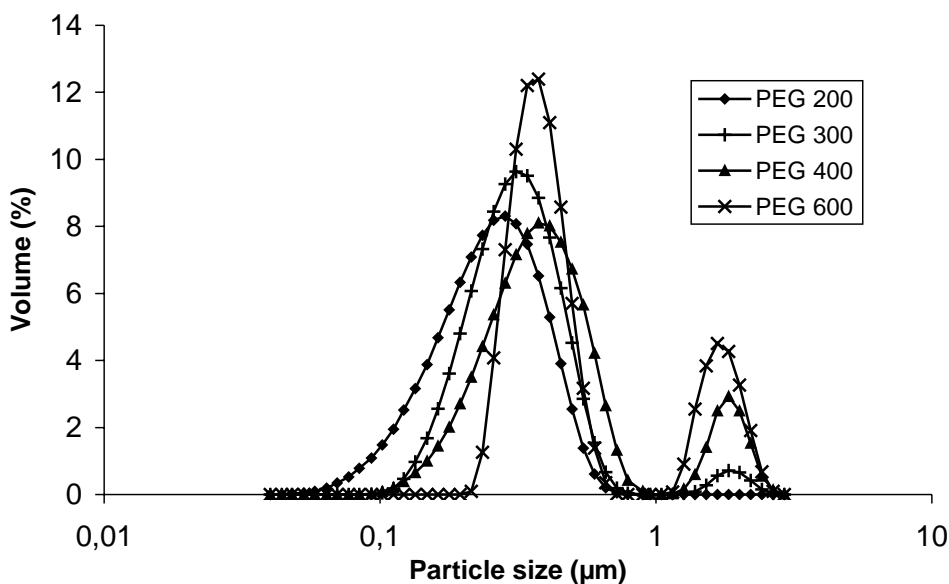


Fig. 4. Particle size distribution of poly(ether urethane) based nanocapsules.

Table 1
Proportions (% w/w) of the different constituents used during the process

Compound	Percentage (w/w) before evaporation	Percentage (w/w) after evaporation
Span® 85	0.06	0.18
Tween® 20	0.11	0.33
α -Tocopherol	0.33	1
Acetone	33.00	ppm
Eau	66.50	98.49

The formation of the polymeric membrane is controlled by the diffusion of the diol present in the water phase through the dense layer. This diffusion is inversely proportional to the water phase viscosity; the polyol/IPDI reactivity is so decreased when molecular weight increases, the capsule shell before maturation should agglomerate forming the second population of microcapsules (Fig. 4).

PEG hydration is another parameter limiting the reactivity with IPDI because the diffusion rate is closely affected by PEG hydration. Kirinèè and Klofutar (1999) have reported that water hydration of PEG

Table 2
Particle size of polyurethanes-based nanocapsules and polyethylene glycol properties

Properties	PEG			
	200	300	400	600
Average molecular weight (g mol^{-1})	190–210	285–315	380–420	570–630
Viscosity range ($\text{mm}^2 \text{s}^{-1}$)				
At 99 °C	3.9–4.8	5.4–6.4	6.8–8.0	9.9–11.3
At 25 °C	41–47	59–66	76–85	130
HLB value	9.3	11.4	13.0	14.6
Density (g cm^{-3}) at 25 °C	1.124	1.125	1.126	1.127
Solubility in water	Complete	Complete	Complete	Complete
Particle size (nm)	218 ± 3	275 ± 32	621 ± 3	615 ± 39

increases with the molecular weight. The hydration number h (the number of bonded water molecules in the hydration polyethylene glycol per mole of solute), is given by Eq. (2) (Kirinè and Klofutar, 1999).

$$h = \frac{d_0(V_\eta - V_{2\phi})M_2}{M_1} \quad (2)$$

where h is the hydration number (number of bonded water molecules per mole of solute), d_0 is the density of water (g cm^{-3}), M_1 is the molecular weight of water (g mol^{-1}), M_2 is the average molecular weight of solute (g mol^{-1}), V_η is the specific volume of hydrated solute ($\text{cm}^3 \text{g}^{-1}$), $V_{2\phi}$ is the apparent specific volume of solute at infinite dilution ($\text{cm}^3 \text{g}^{-1}$).

Moreover, Hong and Park (1999) and Frère et al. (1998) studied the effect of molecular weight increase on microcapsules properties. The size distributions of microcapsules became wider without apparition of a second population (Hong and Park, 1999; Frère et al., 1998). In our system, the mean particle size decreases but the particle size distribution of the nanocapsule population becomes narrower with the apparition of a second population (Fig. 4). The increase of the amount (vol.%) of this second population causes the increase of the mean size diameter. This second population should result on nanocapsules agglomeration.

4.1.2.2. Polyurethanes nanocapsules. Figs. 3 and 5 present the size distribution of low molecular weight diol based polyurethane nanocapsules obtained from ethylene glycol (EG), butanediol (BD), and hexanediol (HD). Their mean particle sizes are very close (232 ± 3), (258 ± 29) and (312 ± 4) nm, respectively.

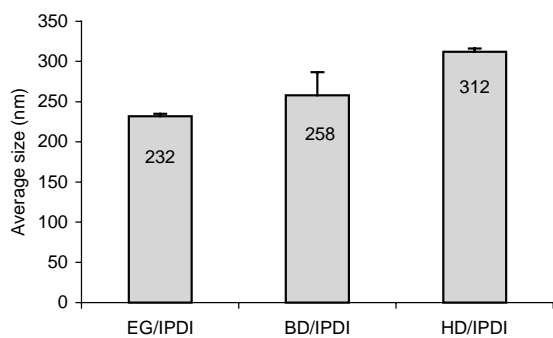


Fig. 5. Mean size diameter of low molecular weight diol-based polyurethane nanocapsules.

The results obtained with low molecular weight monomers confirmed previous observations. It can be noticed that the mean particle size diameter increases with the increase of the molecular weight but there is no particle aggregation.

The higher reactivity of low molecular weight monomers compared to high molecular weight monomers should be the cause of the mean size difference.

4.1.3. Yield of encapsulation and pH measurements

The evaluation of drug loading in nanoparticles needs the separation of the free form of the drug from the encapsulated one. The separation technique most widely used by researchers is ultracentrifugation (Gaspar et al., 1991; Alonso et al., 1991; Ibrahim et al., 1983; Fattal et al., 1989; Fourage et al., 1989; Li et al., 1986; Diepold et al., 1989; Michel et al., 1991). The encapsulated drug is usually measured by complete dissolution of the solid supernatant of nanoparticles in appropriate solvent and ultrasonication during 30 min. The results are summarized in Table 3.

It is observed that α -tocopherol contents in the resulting nanocapsules increase with the increase of the molecular weight of polyols (from 85.6% for EG/IPDI to 92.2% for PEG 600/IPDI).

Our results are in coherent with the literature; Frère et al. (1998) noted that the yield of encapsulation increased with the increase of soft segments molecular weight. The replacement of butanediol with PEG (M_w 600 and 1500) induces an increase of the yield after 4 h of reaction with diphenylmethane diisocyanate (MDI) at 63°C (Frère et al., 1998). Hong and Park (1999) obtained polyurethane-based microcapsules with different molecular weight of polyols, they concluded that the yield of encapsulation was

Table 3
pH measurements and α -tocopherol contents in polyurethane nanocapsules (dissociation isopropanol)

Polyol	Yield of encapsulation (% w/w)	pH
EG	85.6	6.18
BD	87.8	4.68
HD	89.6	5.85
PEG 200	90.6	6.24
PEG 300	90.9	6.58
PEG 400	91.1	6.60
PEG 600	92.2	6.01

proportional to polyols molecular weight (Hong and Park, 1999).

Compared to microcapsules obtained using the classical interfacial polycondensation, the yield of encapsulation is highest in nanocapsules system (5–23% at 25 °C and 63–67% at 63 °C, according to Frères et al., 1998) because in this technique, small amount of oil phase is needed, so we can use directly lipophilic active agents as the inner phase: α -tocopherol, Vitamins (A and E), sun screen agent, for pharmaceutics and cosmetics applications.

4.1.4. Morphologies of nanocapsules

Figs. 6 (1) and 6 (2) shows that polyurethane nanocapsules resulting from the ethylene glycol (EG) and isophorone diisocyanate (IPDI) reaction are spherical. Two populations of nanocapsules with diameters ranging from 40 to 200 nm (a) and from

200 to 900 nm (b), were observed in agreement with granulometric analysis (Fig. 4).

- Spherical and well delimited capsules with an important contrast.
- Broadcast capsules not spherical. There is a net picture quality difference between these two populations of nanocapsules.

After negative colouring, nanocapsules appeared in the form of a spherical white round, on black bottom (Figs. 6 (3) and 6 (4)).

Fig. 7 shows morphologies of poly(ether urethane) nanocapsules with different molecular weights of PEG.

Fig. 7 (1). Black spheres are the capsules. The mean diameter calculated from 94 capsules is around 270 nm. Fig. 7 (2) obtained after negative colouration, shows a population of white spots aggregated

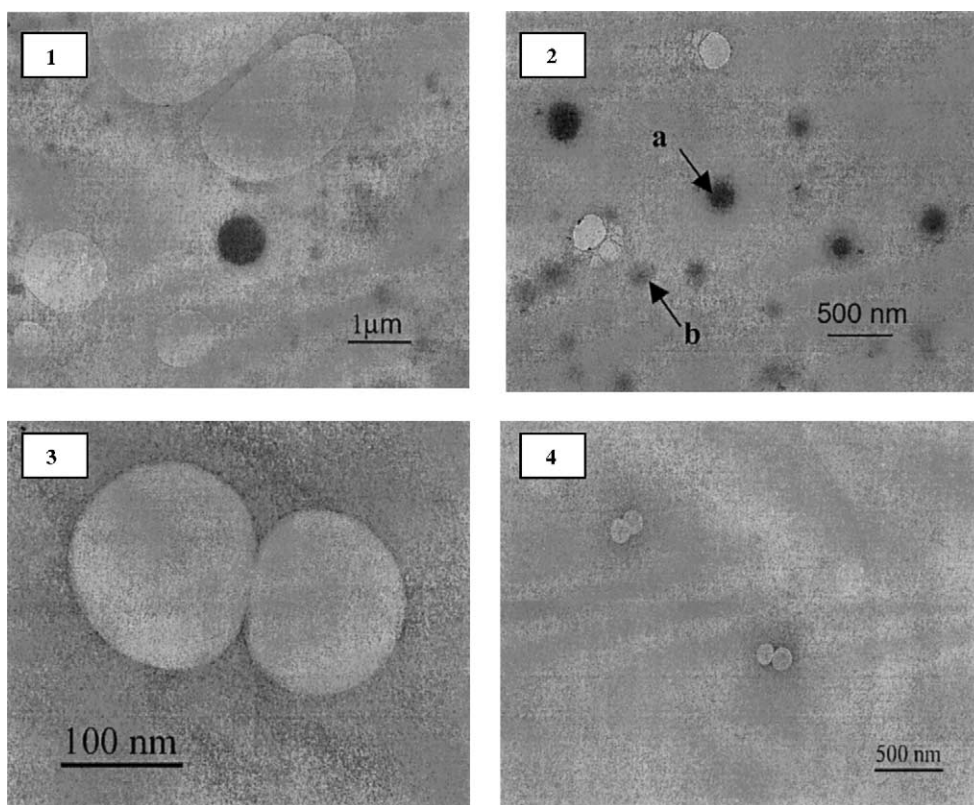


Fig. 6. (1 and 2) Positive observations of EG based nanocapsules; (3 and 4) pictures of two adjacent nanocapsules after negative coloration. The membrane thickness is estimated to 2 nm.

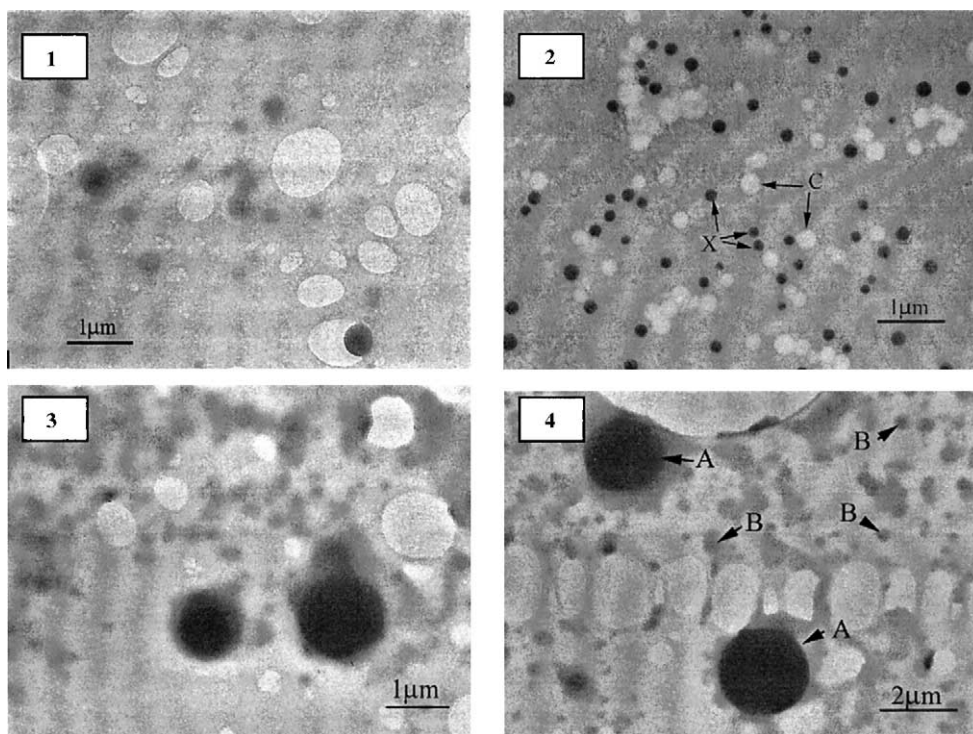


Fig. 7. (1 and 2) PEG 300 direct and negative coloration; (3 and 4) PEG 400 big (A) and small capsules (B).

nanocapsules (C). The second population, which appears as black spots (X) should be an artefact due to the reaction between the colouring solution and the PEG 300 being located in the continuous phase of the preparation. The colouring agent has to be optimized to improve the photographs quality.

Such nanocapsules agglomeration was described also on poly(ϵ -caprolactone) nanocapsules prepared by emulsion-diffusion of solvent (Guinebretière, 2001). This agglomeration can be due to the drying process and to the presence of residual solvents in the moisturized capsules.

On Figs. 7 (3) and 7 (4), microscopic observations show that capsules are spherical. We observe two populations, a population of fine particles (B) with an average size diameter of less than 500 nm present in large number and the other one with an average size diameter of 1–2 μm present in very small number. These results are in harmony with the granulometric analyses, which reveal two populations of capsules.

5. Conclusion

To control nanocapsules properties, we have studied the effect of diols and polyethers molecular weight on polyurethanes and poly(ether urethane) nanocapsules properties: size distribution, yield of encapsulation, pH of the preparation, morphology. Nanocapsules were prepared using a new interfacial polycondensation technique combined with spontaneous emulsification.

The new technique offers numerous advantages compared with the classical interfacial polycondensation. Indeed, classical interfacial polycondensation led to capsules with a mean size diameter varying from 10 to 200 μm . An important quantity of mechanical energy is needed to obtain capsules with weaker size diameter. Thus, there is a risk of monomer hydrolysis by reaction with water and the active agent should diffuse to the continuous phase, decreasing the yield of encapsulation.

The polymer formation was confirmed by FT-IR analysis. Polyurethane nanocapsules could be successfully prepared by the completion of a reaction between diisocyanate and diols and polyethers from the disappearance of an $-N=C=O$ absorption band and the appearance of the $N-H$ and $C=O$ absorption bands.

Nanocapsules were characterized by their particle size distribution, yield of encapsulation, pH and morphologies. A decrease in the molecular weight of diols and polyethers could give nanocapsules with weaker mean diameter and narrow size distribution. Nevertheless, the yield of encapsulation increases with molecular weight increase. Microscopic analysis (TEM) shows spherical particles, the membrane thickness of nanoparticles resulting on EG/IPDI reaction was estimated to 2 nm.

The mean particles size recommended in pharmaceutical and cosmetic formulations destined to topical applications is less than 600 nm. Nanometric systems present an enormous surface area, which makes such substance suitable for important pharmaceuticals and cosmetics applications like topical formulations of lipophilic encapsulated drugs for an homogeneous release. Related to the present work, interfacial polycondensation combined with spontaneous emulsification has been found to have a major role in the production of polymeric nanoparticles with the ability to control the size, the yield of encapsulation and the membrane thickness by varying the molecular weight and the nature of the monomers. These parameters have an increasing importance for pharmaceuticals and cosmetic delivery systems.

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