Water-Soluble Polymers and Gels from the Polycondensation between Cyclodextrins and Poly(carboxylic acid)s: A Study of the Preparation Parameters

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ABSTRACT: Native cyclodextrins (CDx) and some of their derivatives were reacted with poly(carboxylic acid)s (PCAs) [citric acid (CTR), 1,2,3,4-butanetetracarboxylic acid (BTCA), and poly(acrylic acid) (PAA)]. These reactions were carried out in the dry state at a temperature greater than 140°C in air or *in vacuo*. They resulted in water-soluble and insoluble polymers formed by polyesterification between CDx and PCA. In this study, the parameters of the reaction were studied, and their influence on the water solubility or swellability of the obtained polymers was investigated. High reaction temperatures, high PCA/CDx molar ratios, and long reaction times preferably yielded insoluble gels, whereas softer conditions resulted in very soluble polymers. The gels could swell up to 10 times their initial volume in water, and the water-soluble fraction had a solubility of 1 g/mL. A reaction mechanism was proposed that required the use of PCA carrying at least three neighboring carboxylic groups (CTR, BTCA, and PAA), and it was confirmed experimentally by the unsuccessful use of some dicarboxylic acids. A preliminary characterization by Fourier transform infrared spectroscopy and size exclusion chromatography was also conducted. © 2005 Wiley Periodicals, Inc. J Appl Polym Sci 97: 433–442, 2005

Key words: crosslinking; gels; hydrophilic polymers

INTRODUCTION

Cyclodextrin (CDx) polymers are interesting for many fields, such as analytical chemistry, catalysis, the pharmaceutical and food industries, and the treatment of wastewater, as we previously reported.[1–3] The most common method used for their synthesis consists of the crosslinking of CDx with epichlorohydrin.[4–6] This approach has the drawbacks of taking place in concentrated basic media and using epichlorohydrin, a toxic and carcinogen reagent. As a result, the CDx polymers obtained according to this path are not compatible with pharmaceutical or food uses.

In this article, we detail an alternative method that has the advantage of using nontoxic reagents that are water-soluble and that therefore avoids the use of organic solvents. This method is derived from one previously proposed for the graft reaction of CDx onto natural and synthetic fibers,[7–9] as it concerns the same chemical reaction.

As a matter of fact, in 1988, Welch[10] reported that poly(carboxylic acid)s (PCAs) could be efficient crosslinking agents of cellulose, and they were used in the durable press finishing of cotton. In particular, Yang and Wang[11] investigated the mechanism of this reaction and reported that the esterification between PCA and cellulose occurred with the intermediate of a five- or six-membered cyclic anhydride.

Therefore, the most efficient PCAs were those carrying at least three carboxylic groups separated by two or three carbons. As a result, the value of n (which represents the number of carbons present between those carrying the carboxylic groups) in Figure 1 corresponds to 0 or 1. The same authors also investigated the role played by a phosphorous catalyst and reported that it was involved in the formation of the cyclic anhydride intermediate and in the reaction of the latter with cellulose.[12]

Our work consisted of the modification of the reaction reported by Welch[10] through the replacement of cellulose by CDx, another family of carbohydrates, to obtain CDx polymers,[13] which we called polyPCA-CDx.

The reaction resulted simultaneously in two polymer fractions, a water-soluble one and an insoluble
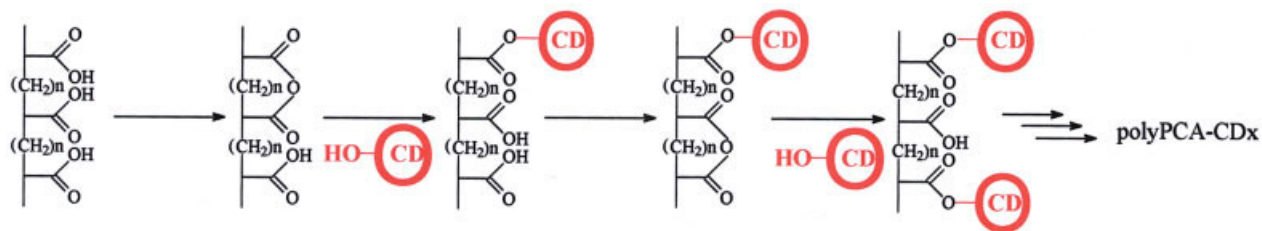
Figure 1 Mechanism of polyesterification between PCA containing at least three carboxylic groups ($n = 0$ or 1) and CDx.

one; the weight ratio of these two forms depended on the experimental conditions. Therefore, this article reports the influence of the reaction time and temperature, the ratio of the reactants, the nature of CDx and PCA, and the influence of the catalyst on the solubility or swellability of this new family of polymers.

EXPERIMENTAL

The polymerization reaction was carried out according to a method previously reported.[13] It involved a PCA—citric acid (CTR), 1,2,3,4-butanetetracarboxylic acid (BTCA), or poly(acrylic acid) (PAA; weight-average molecular weight = 2000)—as a crosslinking agent (they were all from Aldrich, Milwaukee, WI). The CDx samples used in this study were native α-cyclodextrin (α-CD), β-cyclodextrin (β-CD), and γ-cyclodextrin (γ-CD) and a methylated derivative of β-CD (randomly methylated beta cyclodextrin (RAMEB); Cavamax, Wacker Chemie, Burghausen, Germany). RAMEB was randomly dimethylated in positions 2 and 6, and matrix-assisted laser desorption/ionization time-of-flight spectroscopy indicated an average substitution degree of 0.57 (average molar weight = 1303 g/mol). The hydroxypropylated derivative of β-CD (HPβ-CD) had a substitution degree of 0.5 and an average molar weight of 1137 g/mol (Kleptose, Roquette, Lestrem, France). The catalysts used were sodium hydrogen phosphate ($Na_2HPO_4 \cdot xH_2O$), sodium dihydrogen phosphate ($NaH_2PO_4 \cdot 1H_2O$), and sodium hypophosphite ($NaH_2PO_2 \cdot 1H_2O$; all from Aldrich). The aqueous solution was prepared by the solubilization of the catalyst (usually NaH_2PO_4,), CDx, and PCA with respective concentrations of 0.2, 0.09, and 0.45 mol/L under standard conditions.

This solution was then concentrated by evaporation, and the resulting dried mixture underwent a treatment at a temperature between 140 and 170°C. This step was carried out under either reduced or atmospheric pressure in a system connected to a suction pump or not. The polymer was recovered after the addition of water to the flask to solubilize or put into suspension the reaction products. The gel fraction was then filtered off, washed with water and methanol, and dried at 60°C overnight. The soluble fraction was

dialyzed against water (12,000–14,000 Da cellulosic membrane) and then lyophilized. In both cases, a white powder was obtained

The yield of each polymer fraction (soluble and gel) was calculated by the division of the weight of the obtained product by the weight of PCA and CDx in the initial solution. The catalyst was neglected as only traces of phosphorus were recovered in the final products (measured by elemental analysis).

The swelling rate of the gels was measured with a graduated cylinder to which 10 mL of water was added to 0.5 g of a polymer powder. The volume of the swelled gel was measured 1 h later, and the swelling rate was calculated with the ratio V_f/V_i, where V_i and V_f are the volumes before and after the addition of water, respectively.

Fourier transform infrared (FTIR) spectra were recorded with a PerkinElmer Spectrum One spectrometer (Beaconsfield, England) (KBr pellets).

For size exclusion chromatography (SEC), samples were dissolved (0.2% w/v) in an eluent (0.2M NaNO$_3$ and 0.01M NaH$_2$PO$_4$ buffer, pH 7). The columns were two PL aquagel-OH mixed columns (8 μm, 300 × 7.5 mm; Polymer Laboratories), and the flow rate was 1.0 mL/min; detection was conducted with a refractive-index detector, and the calibration was made with pullulan polysaccharide standards.

The CDx polymers were named polyPCA-CDx; PCA could be CTR, BTCA, or PAA, and CDx could be the native CDx or its derivates, as defined previously.

RESULTS AND DISCUSSION

Among the studied parameters involved in the copolymerization of CDs and PCA, Figure 2 reports the influence of the temperature applied during the esterification step, *in vacuo* or in air. On the one hand, a high-temperature treatment (>150°C) involved the preferential formation of insoluble fractions. On the other hand, mainly soluble products were obtained below 150°C. The application of a reduced atmosphere also resulted in an improvement in the yields for both soluble and insoluble polymers. From this experiment, it was established that the synthesis of the soluble form of polyPCA-CDx should be carried out at 140°C
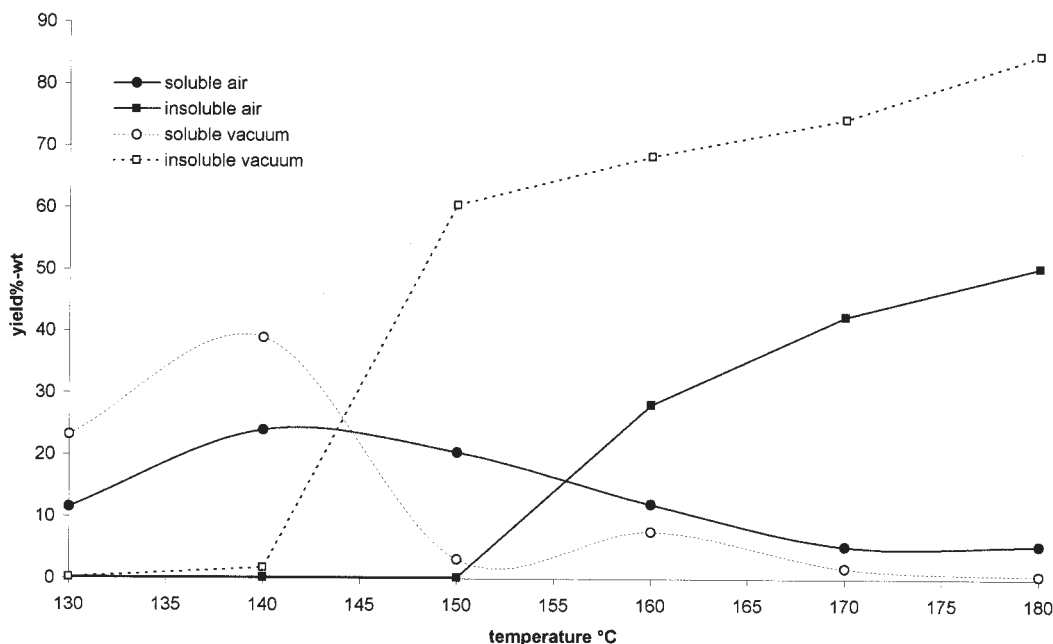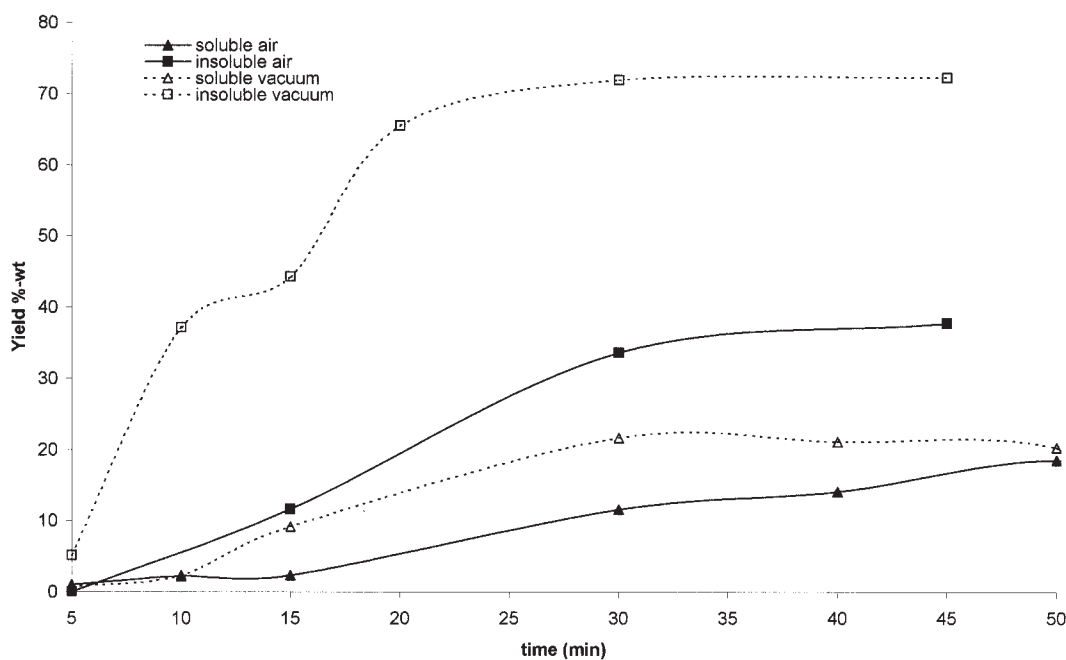
Figure 2 Yield (wt %) in soluble and insoluble polyCTR-β-CD versus the reaction temperature. The copolymers were synthesized under atmospheric conditions or under reduced pressure (reaction time = 30 min).

and that a temperature of 170°C should be applied for the synthesis of the insoluble gel form.

As reported in Figure 3, the yield of the reaction increased with the reaction time within the first 30 min, and then a plateau was reached. The other feature was that the application of vacuum had a very positive influence on the yield of the soluble or insoluble forms of the polymer, especially for the latter.

The results of the two experiences mentioned previously (time and temperature) could be interpreted by the fact that a high temperature and a reduced pressure were factors favoring the removal of the wa-

Figure 3 Yield (wt %) in soluble and insoluble polyCTR-β-CD versus the reaction time. The soluble and insoluble polymers were synthesized at 140 and 170°C, respectively, under an air atmosphere and under reduced pressure.
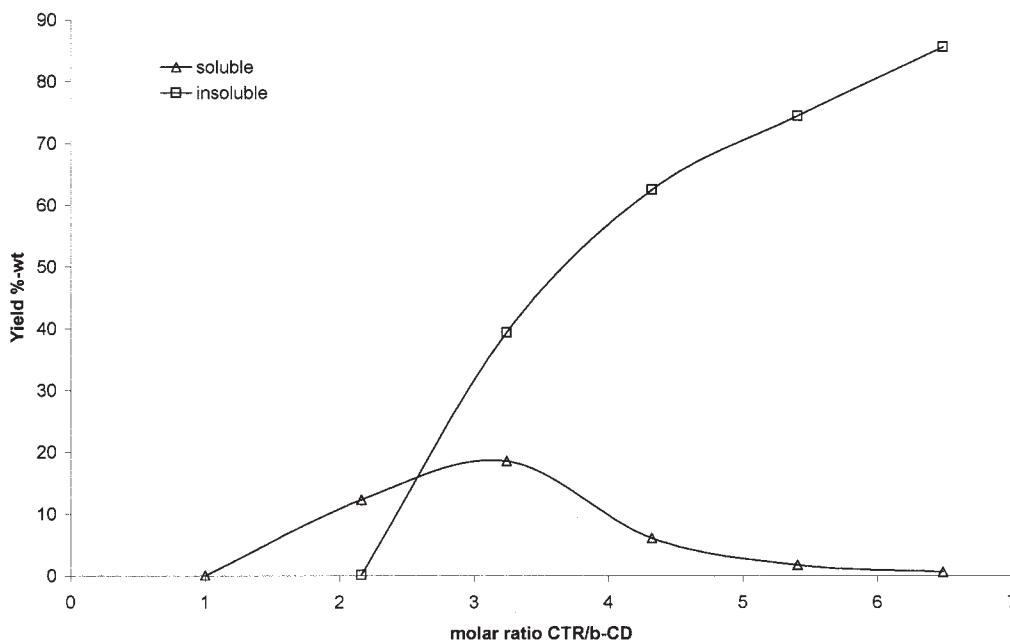
Figure 4 Influence of the CTR/β-CD molar ratio on the yield of the soluble and insoluble fractions of the polymer (temperature = 170°C, reaction time = 30 min, [β-CD] = 0.09 mol/L).

ter formed by the condensation reaction between the anhydride groups and the hydroxyl functions of CDx. In fact, these factors moved the esterification equilibrium in the direction of the ester formation and explained the improvement of the yield of the reaction. In other words, the application of a reduced pressure also allowed the reaction time and the temperature to be reduced, with respect to atmospheric conditions.

In Figure 4, the CTR/β-CD molar ratio (the β-CD concentration was kept constant) in the initial mixture was varied from 1 to 6.5. PolyCTR-β-CD was only obtained when CTR was in excess with respect to β-CD. Therefore, it was very likely that one β-CD unit could react with more than one CTR unit. This could be easily foreseen as one CDx unit carried many esterifiable groups (e.g., 21 hydroxyl groups for one β-CD unit). Therefore, this situation should lead to the crosslinking and gelation of the system according to the theory of the fundamentals of polycondensation reported by Flory[14] and Stockmayer.[15]

Figure 4 shows that an insoluble fraction was collected over a threshold molar ratio of 2 and that the gel yield increased with the ratio. On the other hand, a different response was obtained for the soluble fraction, the yield of which first also increased with the ratio until a value of about 3 and then decreased. In fact, in agreement with the general literature dealing with polycondensation reactions, Figure 4 shows that as the polymerization evolved over the gel point, the insoluble fraction increased at the expense of the soluble one, and more and more soluble macromolecules were incorporated into the gel by crosslinking.[16] In

parallel, the previous literature concerning CDx–epichlorohydrin gels reports that this reaction also led to the simultaneous formation of soluble and insoluble fractions, the ratio of which evolved for the same reasons.[17]

In summary, a slight excess of CTR probably induced a water-soluble polymer of a low molecular weight, and when this excess increased, the crosslinking and extension of the polymer network occurred until a critical size was attained, above which gelation occurred.

This explains why even under the most favorable conditions, the maximum yield of the soluble fraction leveled off at approximately 30% whereas that of the insoluble fraction could reach 90%.

As shown in Figure 5, the nature of the CDx that was polymerized *in vacuo* at 140°C with CTR was varied so that only the soluble fractions of polyCTR-CDx would be obtained. All the polyCTR-CDx samples were obtained with a yield between 17 and 33%, except for polyCTR-RAMEB (only 7%). The lower reactivity of the latter, in comparison with the other CDx samples, was probably due to the lower concentration of hydroxyl groups carried by this methylated derivative of β-CD. As a matter of fact, the mass electrospray analysis of RAMEB (not shown) confirmed that 13 OH groups (out of 21) on average were replaced by methoxy groups.

All three native CDx forms and HPβ-CD were reacted with CTR, BTCA, and PAA. The reaction conditions were set from the aforementioned results to preferably obtain the soluble product (i.e., 140°C, *in vacuo*,
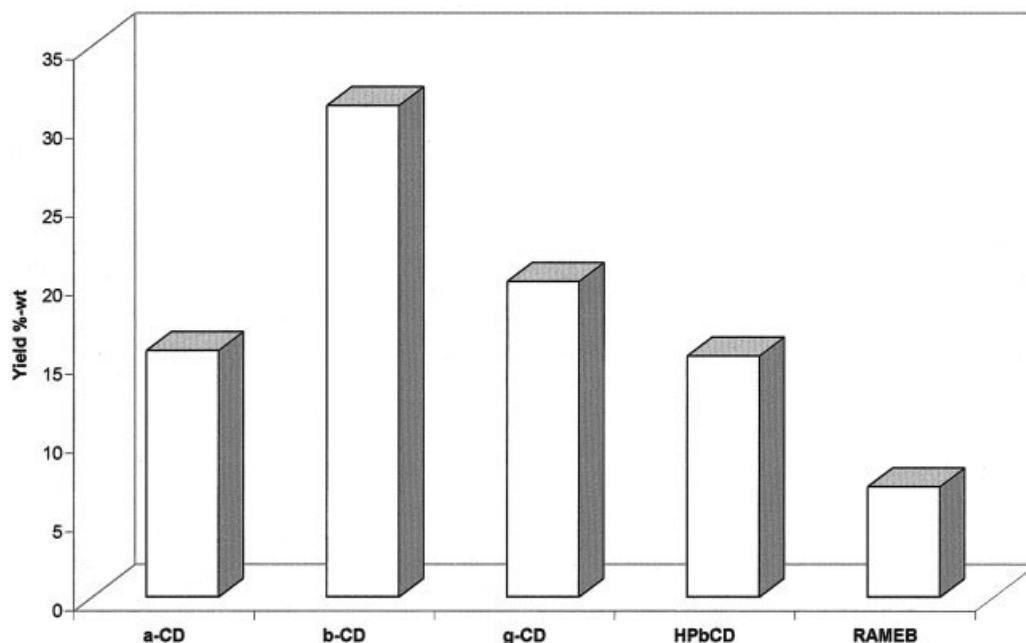
Figure 5 Yield of the soluble fraction of polyCTR-CDx (temperature = 140°C, reduced pressure, CTR/CDx molar ratio = 5, reaction time = 30 min).

and 30-min reaction time). The main feature in Figure 6 is that despite the mild reaction conditions applied, the polymerization carried out with BTCA as the crosslinking agent resulted in a majority in the gelation of the system.

Therefore, BTCA presented better reactivity than the other two PCAs. The same observation was reported by Welch,[10] who compared the efficiency of these three PCAs in the durable press finishing of cellulose. Besides, we also observed the same tendency in the framework of another study that applied this reaction to the graft reaction of textile fibers with CDx.[8]

Oxalic, malonic, and glutaric acids, a series of dicarboxylic acids, were tested and compared with CTR to investigate the influence of the degree of functionalization of PCA. Figure 7 shows that under the applied conditions, a gel of polyCTR-β-CD was abundantly obtained. On the contrary, malonic and glutaric acids only produced a negligible amount of a soluble product, whereas oxalic acid resulted in an insoluble and dark brown oxidized product. Therefore, on the one hand, difunctional carboxylic acids were not appropriate for the polymerization of CDx; on the other hand, it was necessary for the crosslinking agent to bear at least three functional groups, as proposed in the introduction. Furthermore, Figure 1 showed that the linkage of two CDx units by the intermediate of one PCA molecule required the formation of two successive anhydrides issued from three neighboring carboxylic groups.

The influence of the concentration of the catalyst in the solution was investigated and is reported in Figure 8. The variation of Na_2HPO_4 had an effect on the yield of the reaction, especially under normal atmospheric conditions; the addition of 0.1 mol/L of the catalyst increased the yield of the gel 2.5 times.

However, this influence was less evident when a vacuum was applied. Under these conditions, the reaction occurred with a satisfactory yield, even in the absence of a catalyst. We can suppose that the reduced atmosphere was a favorable condition by itself toward esterification.

The solubility measurements of polyCTR-CDx showed excellent results (>1 g/100 mL of water), whatever the nature of the CDx. This was especially noticeable for native β-CD, the solubility of which was only 1.8 g/100 mL at 25°C. On the other hand, the gels swelled in the presence of an excess of water. The swelled gel could reach a volume 12 times that of the dry powder in the most favorable case [Fig. 9(b)]. Besides, we observed that the swellability of a gel decreased with an increasing temperature for synthesis [Fig. 9(a)] and an increasing CTR/CD molar ratio [Fig. 9(b)]. These results can be interpreted in terms of an increase in the crosslinking rates of the polymers, as reported previously. Therefore, high crosslinking rates involved dense polymer networks and low swelling rates; on the contrary, the lower the crosslinking rate was, the higher the swelling rate was. The marked hydrophilicity of both forms of polyPCA-CDx can be explained by the presence of numerous unreacted carboxylic groups in the structure of the polymer. The presence of these ionizable groups is clearly illustrated in Figure 1 and can be explained either by the cleavage of the second anhydride group formed
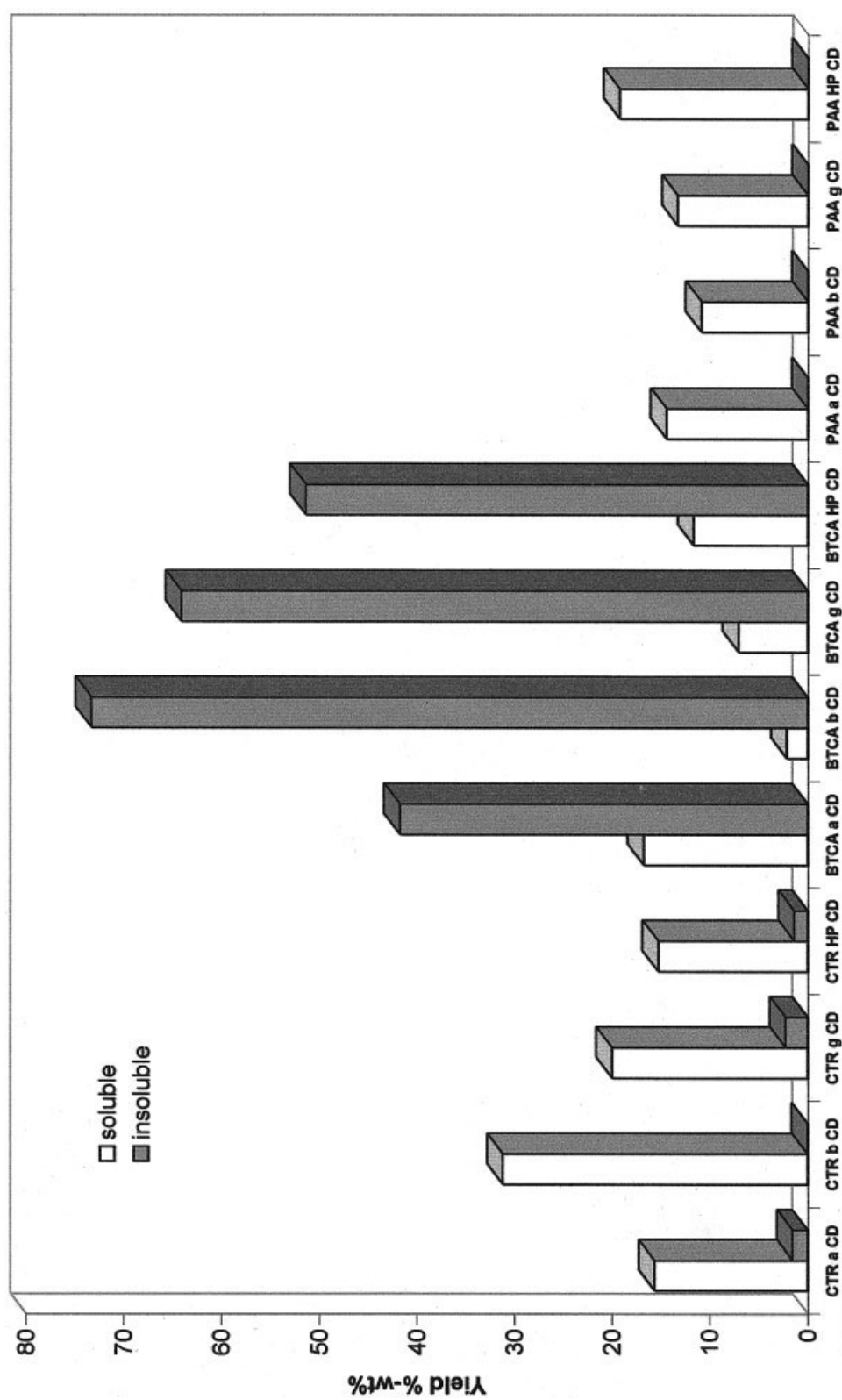
Figure 6 Polymerization between α-CD, β-CD, γ-CD, and HPβ-CD and CTR, BTCA, and PAA (temperature = 140°C, [CTR] = [BTCA] = 0.45M, [PAA] = 1.4M in acrylic groups, reaction time = 30 min, reduced pressure).
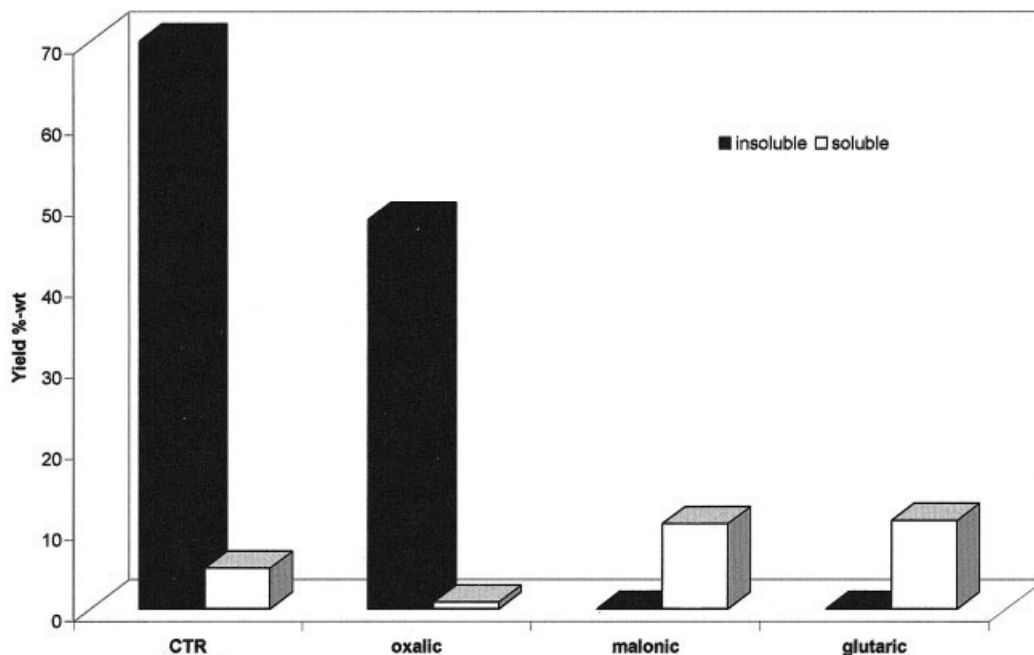
Figure 7 Comparison of CTR and different dicarboxylic acids polymerized with β-CD (temperature = 160°C, PCA/β-CD molar ratio = 5, reaction time = 30 min, reduced pressure).

upon esterification with a second CDx unit or by an incomplete reaction of PCA. The concentration of the remaining COOH groups on polyPCA-CDx is discussed later for the determination of the ion-exchange capacity.

In addition, the alkaline media presented a limitation for these polymers because the gels underwent rapid solubilization through the hydrolysis of the ester linkages.

An analysis of the IR spectra in Figure 10 showed the conversion of the carbonyl groups of the carboxylic acids (1740 cm^{-1}) into esters functions (1850 cm^{-1}). We also identified the ν_{C-H} vibration (2600 cm^{-1}) and the very broad band with respect to the
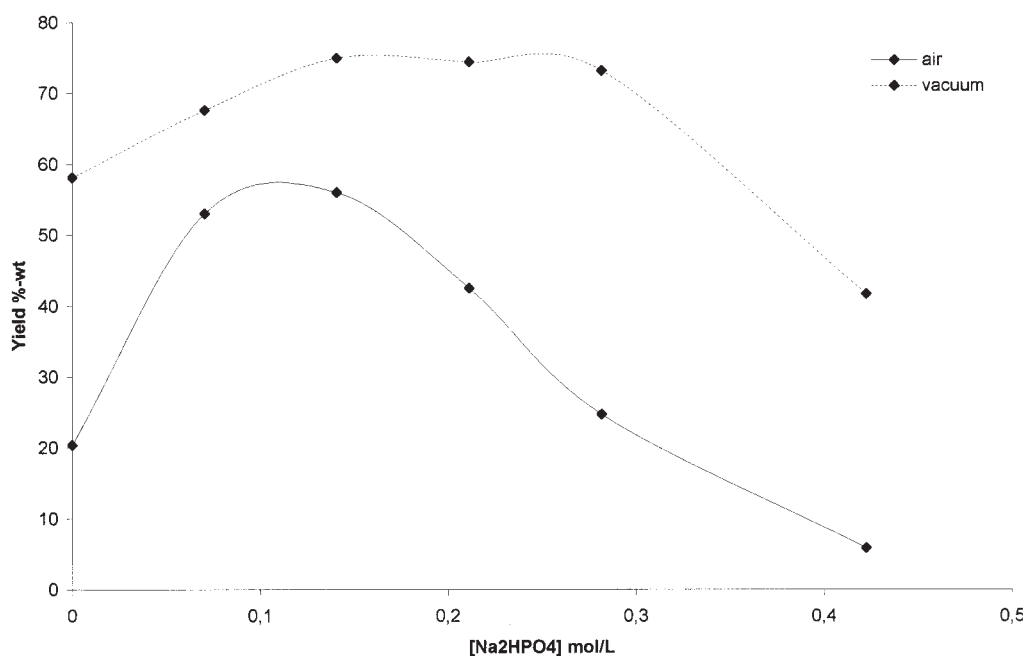
Figure 8 Yield (wt %) in the insoluble fraction of polyCTR-β-CD, versus the catalyst concentration in the solution under normal and reduced pressure (temperature = 170°C, reaction time = 30 min).
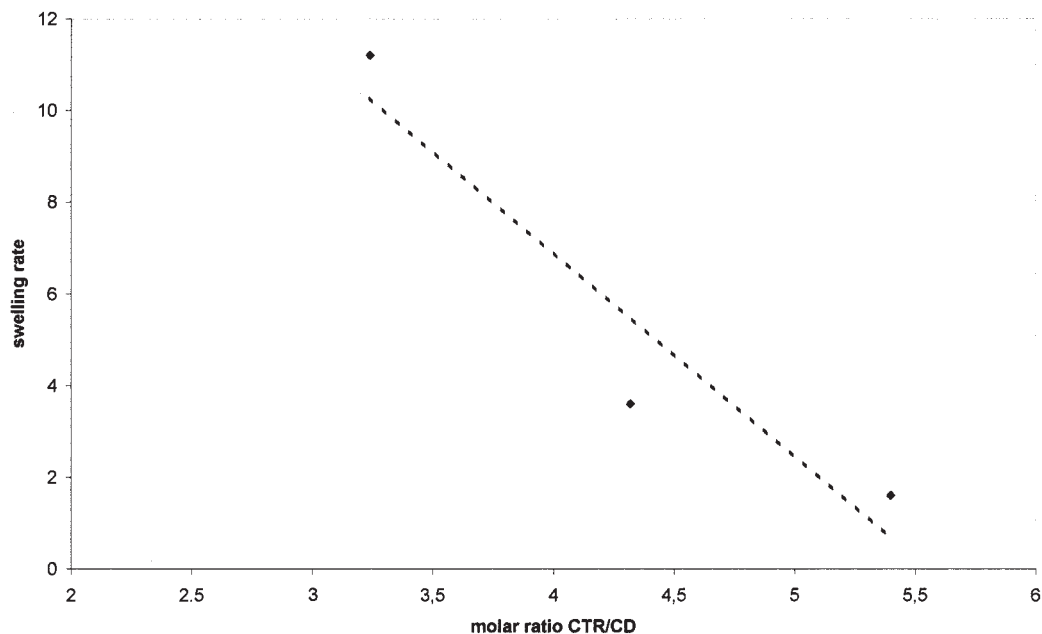
(a)
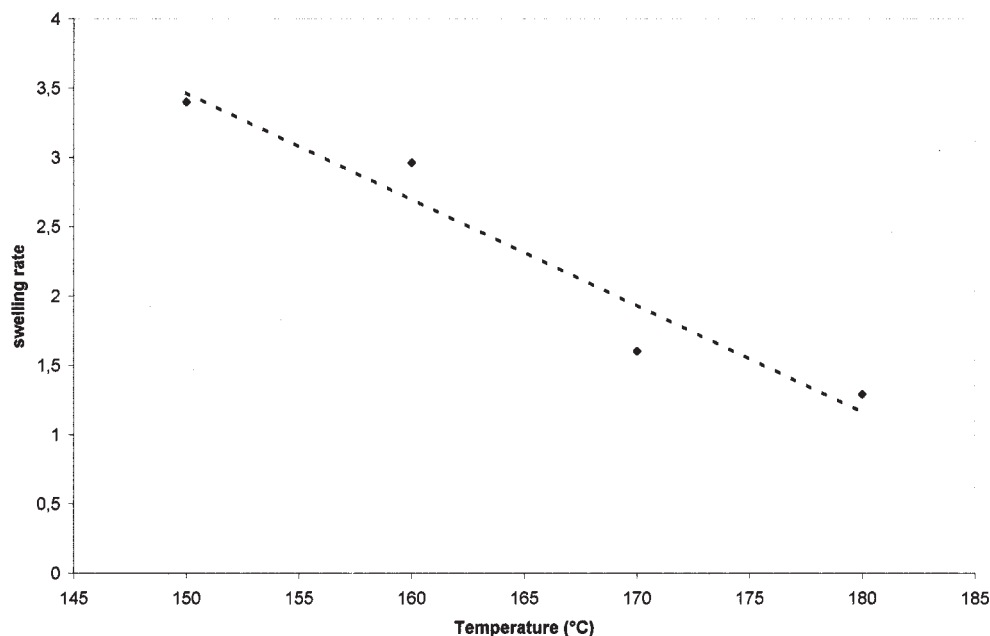
(b)

Figure 9　Influence of the temperature and CTR/CD molar ratio on the swelling rate of gels in water (reaction time = 30 min, *in vacuo*): (a) CTR/CDx molar ratio = 5.5 and (b) temperature = 170°C.

carboxylic acids still present in the two polymers (at 3000 and 3300 cm^{-1} for CTR and BTCA, respectively). Finally, the presence of β-CD in the polymers was revealed by the ν_{C-H} vibration (2900 cm^{-1}) and ν_{C-O} of the ether groups (1000 cm^{-1}).

A preliminary SEC analysis was carried out to determine the macromolecular nature of the soluble fraction. The chromatogram (presented in Fig. 11) revealed that the sample displayed bimodality, with a high-molecular-weight fraction eluting at approximately 14.5 min with a peak molecular weight of approximately 100,000 g/mol. This bimodality was thought to be only the result of the experimental conditions and not the double distribution of the molar masses, as the shearing phenomenon could cause nonspecific interactions with the column. In fact, this was probably due to the viscosity of the polymer on the one hand and to the particle size of the gel (8 μm) on
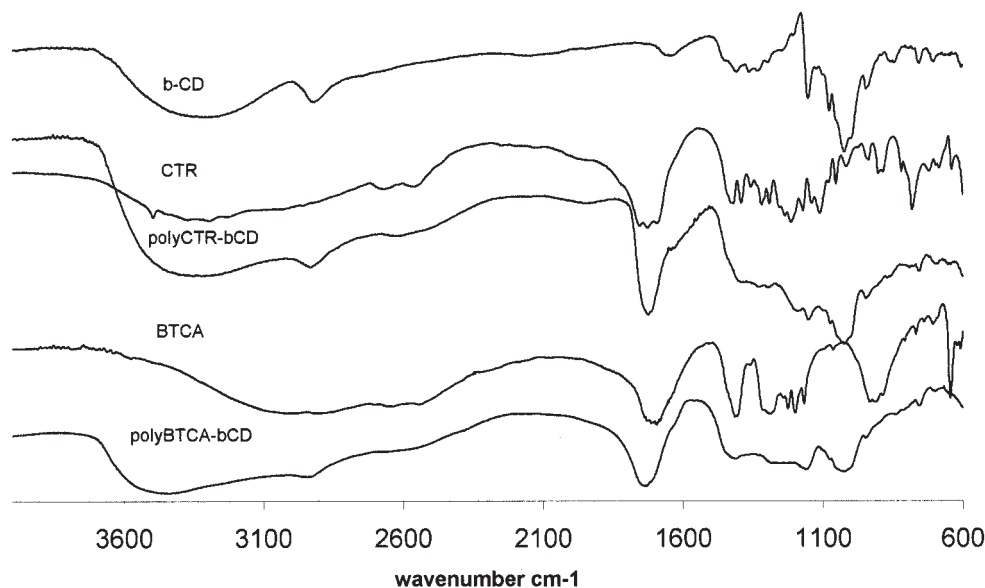
Figure 10 FTIR spectra of β-CD, CTR, BTCA, polyCTR-β-CD, and polyBTCA-β-CD.

the other hand. Shearing should be avoided by the choice of columns with a larger particle size (15 μm), as the void volume would be greater.

Future articles will deal with a more advanced characterization of these products through the use of NMR spectroscopy and other specific techniques of polymer characterization.

CONCLUSIONS

A systematic study of the parameters involved in the polyesterification between PCA and CDx allowed control over the reaction and the characteristics of the final products. This work also helped us to define the optimal conditions that would lead selectively to either the soluble product or the gel with the best possible yield. The gel form could be obtained with a yield higher than 80%, but the soluble form was the result of a compromise of soft conditions that led to a lower yield. All the CDx forms could be polymerized according to this path, as long as they carried enough esterifiable hydroxyl groups. CTR was the most versatile crosslinking agent because, under the defined conditions, it could lead to soluble and insoluble polymers. On the contrary, BTCA preferably yielded some gels, even when soft conditions were applied.

Furthermore, the unsuccessful use of dicarboxylic acids was a confirmation of the proposed mechanism that required PCA carrying at least three neighboring carboxylic groups.

Finally, FTIR and preliminary SEC analysis experiments confirmed the structures and macromolecular structures of the obtained products.
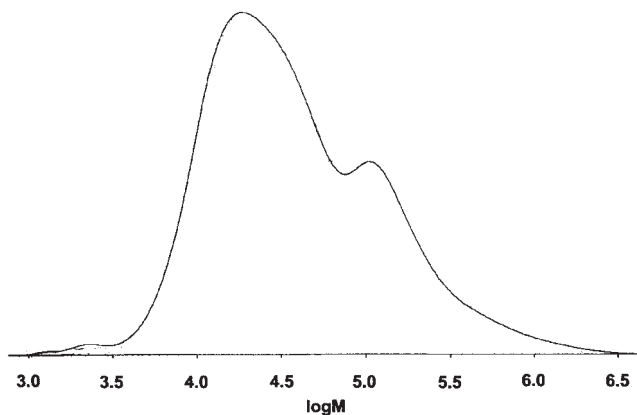

Figure 11 Gel permeation chromatogram of soluble polyCTR-β-CD. M, molecular weight in g/mol.

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