ELSEVIER

Thermochimica Acta 375 (2001) 153–160

thermochimica acta

www.elsevier.com/locate/tca

Thermal analysis behavior of β- and γ-cyclodextrin inclusion complexes with capric and caprilic acid

Marcia M. Meier, Marilde T.B. Luiz, Bruno Szpoganicz, Valdir Soldi*

Laboratorio de Polimeros (POLIMAT), Departamento de Química,
Universidade Federal de Santa Catarina, Florianópolis, SC 88040-900, Brazil

Received 14 November 2000; received in revised form 7 March 2001; accepted 10 March 2001

Abstract

The inclusion complex of capric (C_{10}) and caprilic (C_8) acids with β- and γ-cyclodextrins (CDs) was analyzed, in the solid state, by differential scanning calorimetry (DSC), thermogravimetry (TGA), and infrared spectroscopy (FT-IR). Special attention was paid to the acid behavior in terms of the quantity incorporated and the thermal stability. The results showed that the maximum amount of incorporated acid in β-CD occurred at molar ratio (CD:acid) of 1:1 and 1:1.5 for C_{10} and C_8, respectively. For the same acids in γ-CD, the proportions increased to 1:1.5 (C_{10}) and 1:2 (C_8). The heat for the water volatilization was higher in γ-CD (ca. 91 cal g^{-1}) than β-CD (ca. 52 cal g^{-1}) systems, for both acids, probably because of the high cavity size of γ-CD. Although, both systems improved additional thermal stability with the complex formation, the acids acquired a higher thermal stability in the β-CD inclusion complex.

Keywords: Cyclodextrins; Capric acid; Caprilic acid; Inclusion complex; Thermal stability

1. Introduction

Cyclodextrins (CD) are host molecules that can form inclusion complexes with a great variety of guest molecules [1–6]. They are defined as torus-shaped cyclic oligosaccharides, consisting commonly of six (α-CD), seven (β-CD) or eight (γ-CD) glucose units linked by 1,4-α-glucosidic bonds [2,7]. The inclusion of a guest molecule in the cyclodextrin cavity may modify physico-chemical properties, such as solubility [5] and thermal stability [8].

In general, techniques, such as UV [3], NMR [9], FT-IR [4], conductimetry, potentiometry [10,11] and X-ray diffraction [1] have been used to analyze the inclusion complex formation. Recently, thermal analysis has also been used in studies of inclusion complexes [4], but only a few researchers have viewed thermal decomposition quantitavely [5,8]. Novák et al. [5], for example, studied the inclusion complexes formed by racemic and optically-active mandelic acid with α-, β- and γ-cyclodextrins. It was observed that the decomposition of the complexed mandelic acid occurs 50°C above that of the free mandelic acid. The thermal decomposition takes place in several steps due to the formation of complexes with different molar ratio and consequently with different thermal stability.

The thermal decomposition of solid inclusion complexes of ferrocene and derivatives with β-CD was studied by Yilmaz et al. [8]. With the formation of the inclusion complex, the melting peaks of ferrocene and derivatives were not observed. The inclusion complex

---

* Corresponding author. Tel.: +55-48-331-9230;
fax: +55-48-331-9711.
E-mail address: vsoldi@qmc.ufsc.br (V. Soldi).

PII: S0040-6031(01)00514-7

is also responsible for the increase of the thermal stability of the ferrocene derivatives.

Luiz and coworkers reported that β-CD reduces the goaty flavor in goat's milk [12,13], due to the formation of inclusion complexes between β-CD and molecules, such as short chain fatty acids [14,15]. The inclusion complex between short chain fatty acids and β-CD was studied recently in aqueous solution [3,16]. However, although the study of this complex in solid state seems very important, no reports have been found in the literature.

The aim of this work was to analyze the inclusion complex formation between capric (decanoic, C_{10}) and caprilic (octanoic, C_8) acids and β- and γ-CD, in the solid state. The main idea was to analyze the acid behavior in terms of the quantity incorporated and the thermal stability. The molar ratio (fraction) in which the maximum amount of encapsulated acid in each CD occurred was determined by differential scanning calorimetry (DSC). The thermal decomposition behavior and the relative stability of both acids, before and after their inclusion in β-CD and γ-CD cavities, were investigated by thermogravimetric (TGA) analysis and infrared spectroscopy (FT-IR).

2. Experimental

2.1. Materials

The cyclodextrins were supplied by Cerestar (USA) and were recrystallized in water. Capric and caprilic acid, 99%, were purchased from Fluka and were used without further purification.

2.2. Preparation of solid complexes

The inclusion complexes were prepared by adding the acid to a saturated cyclodextrin aqueous solution in a molar ratio (CD:acid) range of 1:0.57 to 1:2, at approximately 50°C. Each system was stirred for 6 h and the solvent was evaporated at room temperature. The samples were dried under vacuum and kept in a dessecator for analysis.

2.3. Methods

Thermal analysis were carried out using a Shimadzu system (DSC-50 and TGA-50) at a heating rate of 10°C min^{-1} and N_2 atmosphere (50 ml min^{-1}). Samples with average mass of 5 and 12 mg were used for DSC and TGA analysis, respectively. Standard indium (156.6°C) and hydrate calcium oxalate were used for DSC and TGA calibration, respectively.

The residual products of the thermal decomposition reaction were analyzed by FT-IR using Perkin-Elmer (16PC) equipment with a resolution of 4 cm^{-1}. The samples were prepared in the form of compressed KBr disks. The presence of acid (C_8 or C_{10}) in the inclusion complex at different decomposition stages was analyzed considering the characteristic bands at 1712 cm^{-1} (stretching C=O) and 1648 cm^{-1} (cyclodextrin band, [4,5]) from acid and cyclodextrin, respectively.

3. Results and discussion

3.1. Differential scanning calorimetry

Fig. 1 represents the DSC curves for β- and γ-CD, C_8 and C_{10} acids, showing only an endothermic transition at ca. 120°C for the CD, corresponding to the water content. Endothermic peaks at 13.9 and

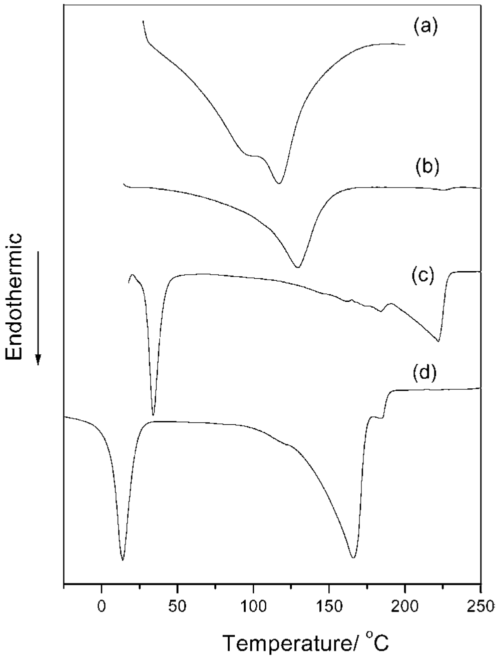

Fig. 1. DSC curves for: (a) γ-CD; (b) β-CD; (c) C_{10} and (d) C_8.

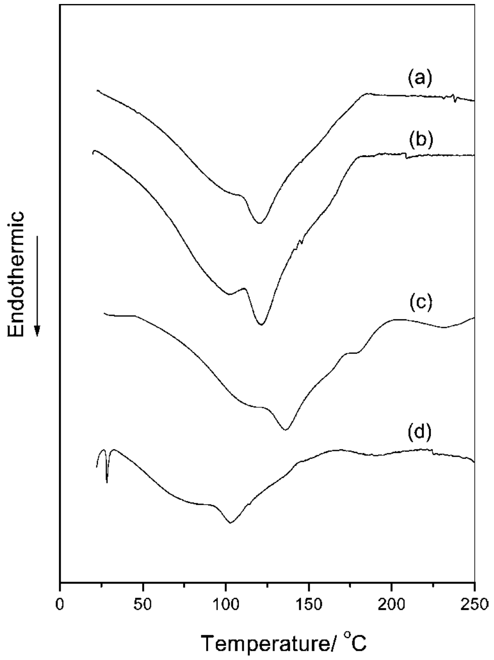

Fig. 2. DSC curves of β-CD/C_{10} system at different molar ratios (CD: acid): (a) 1:0.57; (b) 1:0.91; (c) 1:1 and (d) 1:1.14.

33.9°C were observed for C_8 and C_{10}, respectively, due to the melting transitions.

Fig. 2 shows the DSC curves of different molar ratio of β-CD/C_{10} system. Table 1 shows the absorbed heat related to the endothermic peaks of the pure components and the inclusion complex at different molar ratios (CD:acid). For the CDs and the inclusion complexes, the determined energy is related with the dehydration of water molecules.

From the literature [17], it is known that if a guest molecule forms an inclusion complex with cyclodextrin, and interaction with other components does not occur, there is no crystalline guest structure to absorb energy. Then, the inclusion complex formation can be confirmed by the comparative analysis of the DSC curves of pure CD, guest molecule and the complex.

The endothermic peak observed at 28.3°C (Fig. 2, curve d) corresponds to the melting peak of the C_{10} acid, indicating that in the molar ratio (β-CD:C_{10}) 1:1.14 the acid was not totally encapsulated by β-CD. A total acid encapsulation (corresponding also to a maximum) occurred when the proportion β-CD:C_{10} was equal to 1:1 (Fig. 2c). At this fraction, the melting acid transition was not observed.

Table 1

DSC results at different molar ratios for the study of inclusion complexes at a heating rate of 10°C min^{-1} and nitrogen atmosphere (50 ml min^{-1})

System	Molar ratio (CD:acid)	Peak (°C)	Heat (cal g^{-1})
β-CD/C_{10}	0:1	34, 221	35.1, 106.1
	1:0	129	91.0
	1:0.57	120	53.8
	1:0.91	121	52.4
	1:1[a]	115, 127	51.9
	1:1.14	28, 103	0.4, 36.7
β-CD/C_8	0:1	14, 166	36.3, 117
	1:0.8	114	80.8
	1:1	110, 140	55.0
	1:1.2	114, 133	73.0
	1:1.5[a]	~100, 128	52.8
	1:1.7	11, 119	0.4, 71.4
γ-CD/C_{10}	1:0	120	65.4
	1:1	125	87.2
	1:1.3	135	79.5
	1:1.5[a]	106	91.6
	1:1.8	~28, 119	91.8
γ-CD/C_8	1:1	138	90.7
	1:1.5	130	95.6
	1:2[a]	106	90.3
	1:2.3	10, 108	0.4, 95.0

[a] Maximum encapsulated acid.

The same analysis was performed for β-CD/C_8, γ-CD/C_{10} and γ-CD/C_8 systems and the results showed a maximum acid encapsulation at the proportions (CD: acid) of 1:1.5, 1:1.5 and 1:2, respectively. Two points are in evidence considering the above results. First, the amount of encapsulated C_8 in β-CD was 50% higher than of the C_{10}. Similar behavior was observed for the γ-CD/acid system in which the maximum amounts of encapsulated C_{10} and C_8 were 1.5 and 2, respectively for a single molecule of γ-CD. The above results are apparently related with the differences in the chain size of the two acids. Another aspect is related to the cavity size of β- and γ-CD. The increase of the amount of encapsulated acid in the γ-CD can be due also to the higher cavity size in comparison with β-CD.

The DSC curves of β-CD/C_{10} (Fig. 2) and β-CD/C_8 (not shown) systems exhibit small endothermic peaks (like a shoulder) in the range 80–150°C, suggesting that the energies for dehydration of water molecules are different. It is known that some of the water molecules included in the CD cavity are able to form hydrogen bonding with carboxylic acid groups (guest molecules), thus changing the dehydration energy. Similar behavior was reported by Li and coworkers [18], considering the DSC curves of β-CD/cinnamic aldehyde inclusion complex.

Some general features can be recognized from Table 1. For the γ-CD/C_{10} (1:1.5) and γ-CD/C_8 (1:2) systems, the dehydration temperatures are lower than the dehydration temperature of pure γ-CD, indicating that the inclusion of capric and caprilic acids into CD cavities results in the weakening of the bonds between the remaining water molecules. Yilmaz et al, [8] observed similar behavior for β-CD/ferrocene derivative inclusion complexes.

The heat necessary for the volatilization of the water molecules from the inclusion complexes with a maximum quantity of encapsulated acid is 51.9 and 91.6 cal/g for β-CD and γ-CD systems, respectively. The values of 51.9 cal/g for β-CD/C_{10} and 52.8 cal/g for β-CD/C_8 inclusion complexes suggest a volatilization of approximately the same number of water molecules from these systems. The heat value increases to ca. 91 cal/g in the γ-CD inclusion complexes, probably due to the γ-CD cavity which can hold more water molecules than the β-CD cavity. Systems with uncomplexed acid exhibit a lower fusion enthalpy, attributable to a better dispersion of the acid microcrystals in the CD [4].

3.2. Thermogravimetry

The TGA and DTG curves for pure β-CD and β-CD/C_{10} (1:1), γ-CD and γ-CD/C_{10} (1:1.5) inclusion complexes are shown in Figs. 3 and 4, respectively. The decomposition stages, temperature ranges,

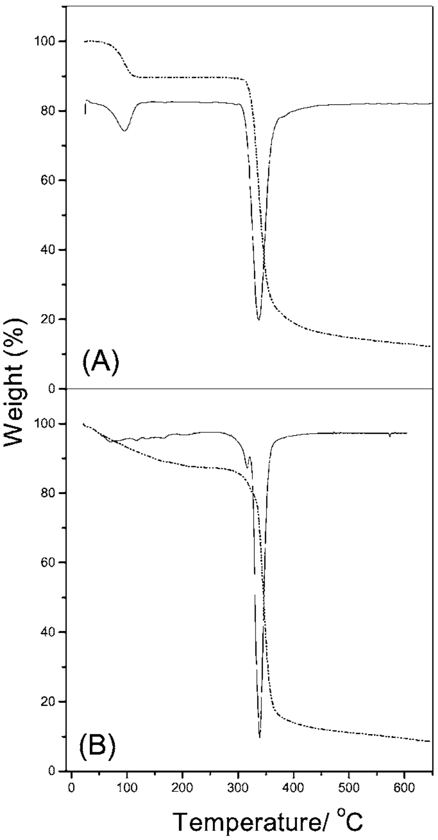

Fig. 3. TGA (dashed line) and DTG (solid line) curves of (A) β-CD and (B) β-CD/C_{10} inclusion complex.

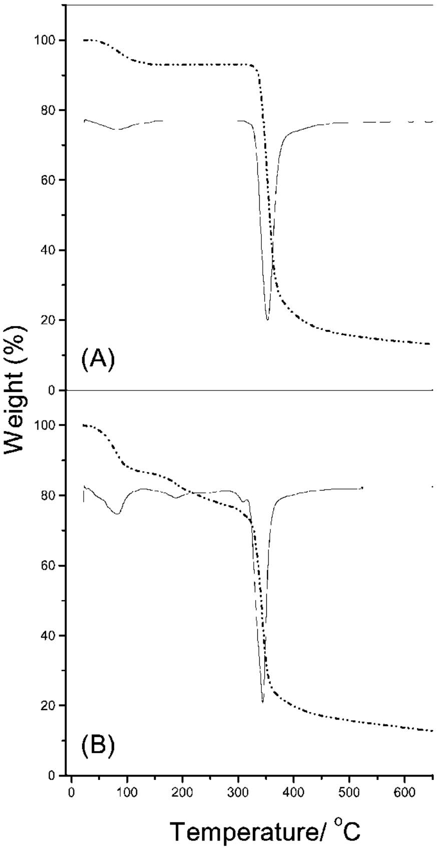

Fig. 4. TGA (dashed line) and DTG (solid line) curves of (A) γ-CD and (B) γ-CD/C_{10} inclusion complex.

Table 2
Thermogravimetric results considering the TGA curves at 10°C min^{-1}, for pure β-CD, γ-CD, C_{10} and C_8

System	Stage	TGA (temperature range, °C)	DTG_{min} (°C)	Weight loss (%)
β-CD	1	33–130	94	10.3 (7.3 mol)
	2	291–850	338	77.5
γ-CD	1	30–213	83	7.8 (6.2 mol)
	2	288–850	342	79.4
C_{10}	1	117–243	224	99.2
C_8	1	75–225	196	99.4

experimental and estimated weight loss of pure components and inclusion complexes are presented in Tables 2 and 3, respectively.

The first stages of thermal decomposition for pure β-CD (Fig. 3A) and γ-CD (Fig. 4A) are related to the dehydration at the temperature range of 33–130°C, with 10.4% of water weight loss (7.3 mol), and 30–213°C, with 7.8% of water weight loss (6.2 mol), respectively. The second stages are related to the decomposition of CD structure, and weight losses of 77.5 and 79.4% were observed, indicating that residual masses of ca. 15 and 10% in the β- and γ-CD samples remained. The decomposition stages discussed above have been described elsewhere [4,5,8,19]. Pure C_8 and C_{10}, on the other hand, exhibit a single decomposition stage, due to the acid volatilization. At 225 and 243°C, the C_8 and C_{10} acids (respectively) are totally volatilized.

The water contents determined for pure β- and γ-CD was 7.3 and 6.2 mol, respectively (Table 2). Connors [7] reported the presence of 11 or 12 water molecules in β-CD, but this number was changeable depending on the relative humidity. On the other hand, γ-CD is able to crystallize with 7–8 molecules of water.

In this work, β- and γ-CD were recrystallized from concentrated solutions and allowed up to 4 days for the crystal formation. Due to the organized structure in the

Table 3
Thermogravimetric results considering the TGA curves at 10°C min^{-1}, for β-CD/C_{10} (1:1), β-CD/C_8 (1:1.5), γ-CD/C_{10} (1:1.5) and γ-CD/C_8 (1:2) inclusion complexes

Inclusion Complex	Stage	TGA (Temperature range, °C)	DTG (°C)	[Weight loss (%)]		Molar quantity[a] [(mol)]
				Experimental	Estimated[a]	
β-CD/C_{10} (1:1)	1	22–232	93	12.2		5.8 (H_2O)
	2	232–327	320	7.8	12.0	1.0 (C_{10})[b]
	3	327–637	346	71.0		
β-CD/C_8 (1:1.5)	1	25–135	98	5.7		4.3 (H_2O)
	2	136–260	154	4.8	13.7	0.5 (C_8)[c]
	3	266–632	346	80.2		
γ-CD/C_{10} (1:1.5)	1	30–130	84	13.0		11.2 (H_2O)
	2	134–283	189	9.6	11.0	
	3	295–311	309	1.9		1.2 (C_{10})[c]
	4	316–650	343	61.0		
γ-CD/C_8 (1:2)	1	23–134	91	14.3		12.6 (H_2O)
	2	136–255	178	9.7	15.0	
	3	255–302	281	2.3		1.5 (C_8)[c]
	4	302–643	335	58.0		

[a] According to the initial mass used for the complex preparation.

[b] Approximately 0.3 mol of the C_{10} decomposed in the first stage.

[c] The remaining acid decomposed in the last stage, in agreement with the FT-IR results.

crystalline form of β- and γ-CD, fewer water molecules could be incorporated in the structure. However, the inclusion complexes with the acids C_8 and C_{10} did not formed crystalline structures, permitting a higher hydration and thus justifying the significant difference between the water content of the inclusion complexes and that of the pure cyclodextrins. Another aspect is related to the formation of hydrogen bonding between the water molecules and the carboxylic groups of the acids C_8 and C_{10}. Considering that the content of encapsulated acid in γ-CD is higher than in β-CD, a higher content of water molecules is expected in the complexes with γ-CD, as shown in Table 3.

For the inclusion complexes studied in the present work, the decomposition reactions (TGA curves) suggest three mass-loss stages corresponding to: (i) water release; (ii) acid volatilization; and (iii) the CD decomposition. The above behaviour was observed in the TGA/DTG curves for β-CD/C_{10} (1:1) inclusion complex (Fig. 3B). The FT-IR analysis of β-CD/C_{10} samples submitted to different heat temperatures was used to demonstrate at which temperature range the C_{10} volatilization occurred. As may be observed in Fig. 5A, the band intensity at 1712 cm^{-1} (corresponding to the acid stretching C=O) decreased in comparison with the band at 1648 cm^{-1} (cyclodextrin band), at a temperature range of 25–200°C, suggesting a partial acid decomposition until ca. 200°C. These results confirm that part of C_{10} is released in the first decomposition stage (Table 3) and part of it is released in the second stage. The third stage represents only the decomposition of β-CD structure.

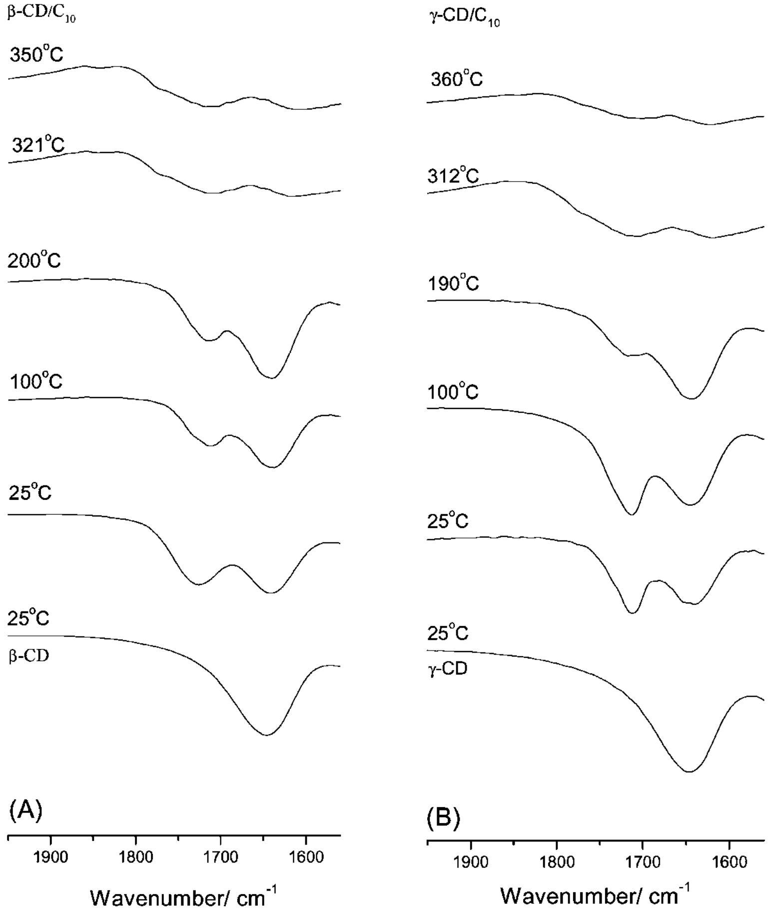

Fig. 5. FT-IR spectra at different temperatures of: (A) pure β-CD and β-CD/C_{10} (1:1) inclusion complex; (B) pure γ-CD and γ-CD/C_{10} (1:1) inclusion complex.

The release of part of C_8 from the β-CD/C_8 (1:1.5) complex occurred at 136–260°C with 4.8% of weight loss, instead of 13.7% which was estimated according to the initial mass used for the complex preparation. Part of the acid (ca. 9%) volatilized above 260°C, suggesting an increase in the acid thermal stability with the inclusion complex formation. The residual acid apparently decomposed at the same temperature range as the β-CD. The above results are in agreement with the FT-IR analysis (not shown).

The TGA/DTG curves for γ-CD and γ-CD/C_{10} (1:1.5) inclusion complexes are shown in Fig. 4. For both systems, the first decomposition stage is related to the water release which corresponds to 7.8 and 13.0% of weight loss for γ-CD and γ-CD/C_{10}, respectively. In Fig. 4A, the second decomposition stage represents the weight loss for pure γ-CD. For the γ-CD/C_{10} (1:1.5) inclusion complex, on the other hand, the second and third mass-loss stages, at temperature ranges of 134–283°C and 295–311°C, represent the acid volatilization. The CD structure decomposition occurred at the fourth decomposition stage. Similar behavior was observed for the γ-CD/C_8 inclusion complex.

As observed in Table 3 for the acid decomposition in the γ-CD inclusion complexes, the percentages of weight loss up to ca. 300°C are consistent with the estimated values (ca. 11 and 15% of C_{10} and C_8, respectively) considering the initial mass used in the preparation of the complex. The above results are in agreement with the FT-IR shown in Fig. 5B for the γ-CD/C_{10} inclusion complex, in which at 190°C only a shoulder corresponding to the acid C=O stretching at 1712 cm^{-1} was observed. The shoulder suggests that a small amount of C_{10} acid remained incorporated in the γ-CD cavity. The same behavior was observed for the γ-CD/C_8 inclusion complex (not shown). The percentages of water and acid loss (Table 3) were estimated as molar quantities which are in agreement with the decomposition stages described earlier. For example, in the β-CD/C_8 (molar ratio, 1:1.5) inclusion complex, 4.3 mol of water was lost in the first stage and 0.5 mol of C_8 was volatilized in the second stage. The remaining 1.0 mol of C_8 was probably volatilized in the last stage as observed by FT-IR. Similar considerations could be made for the other complexes. The molar quantities for the corresponding CD decomposition were not estimated because a residual mass was observed in all the TGA curves.

Table 4
Percentage of C_{10} and C_8 that remained encapsulated in the CD cavities at over 243 and 225°C, respectively.

Complex	Temperature (°C)	Acid (%)
β-CD/C_{10}	>243	62
β-CD/C_8	>225	71
γ-CD/C_{10}	>243	31
γ-CD/C_8	>225	46

The above results suggest that in the γ-CD and β-CD inclusion complexes the volatilization of C_{10} and C_8 occurs in two stages due to the formation of complexes with different molar ratio and consequently with different thermal stability. Novák et al. [5] observed similar behavior in the β-CD/mandelic acid inclusion complex.

In order to analyze whether the C_{10} and C_8 acids had gained additional thermal stability after encapsulation in the CD cavities, we summarized in Table 4 the acid percentage that remained encapsulated above 243 and 225°C, which are the temperatures corresponding to the total volatilization of pure C_{10} and C_8, respectively, as shown in Table 2. We observed that 62 and 71% of C_{10} and C_8, respectively, remained inside the β-CD cavity, and that only 31 and 46% remained in the γ-CD cavity after the mentioned temperatures. In comparison with pure C_{10} and C_8, both CD cavities brought additional thermal stability to the acids after encapsulation. Therefore, the thermal stability in the β-CD cavity was higher than that of the γ-CD cavity, probably because of a strong association with the acids.

4. Conclusions

The formation of inclusion complexes, with a maximum amount of incorporated acid, occurred at a molar ratio (CD:acid) of 1:1 and 1:1.5 for β-CD/C_{10} and β-CD/C_8, respectively. For γ-CD/C_{10} and γ-CD/C_8, the amount of incorporated acid was increased and the molar ratios were 1:1.5 and 1:2. The heat related to the water volatilization in the β-CD complexes was ca. 52 cal/g for both acids. In the γ-CD complexes, the heat was ca. 91 cal/g for both acids, indicating the volatilization of a higher number of water molecules than occurred in the β-CD systems. The observed behavior is related with a high cavity size for γ-CD. The thermogravimetric results showed that C_{10} and C_8, encapsulated in β-CD, volatilized at higher temperatures than the free acids did. In the γ-CD systems, on the other hand, the acid thermal stability did not increase by the same proportion as it did in the β-CD systems. Despite the difference, the acids gained an additional thermal stability with the formation of inclusion complex.

Acknowledgements

The authors wish to express their sincere appreciation to Cerestar (USA) for providing the cyclodextrins. This research was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

References

[1] A. Zornoza, C. Martín, M. Sánchez, I. Vélaz, A. Piquer, Int. J. Pharmaceutics 169 (1998) 239.
[2] J. Szejtli, Chem. Rev. 98 (1998) 1743.
[3] C.A. Georgiou, S.G. Skoulika, M.G. Polissiou, J. Inclusion Phenomena Macrocyclic Chem. 34 (1999) 85.
[4] J.R. Moyano, M.J. Arias, J.M. Ginés, J.I. Pérez-Martínez, P. Muñoz, F. Giordano, J. Thermal Analysis 51 (1998) 1001.
[5] Cs. Novák, M. Fodor, G. Pokol, V. Izvekov, J. Sztatisz, M.J. Arias, J.M. Ginés, J. Thermal Analysis 51 (1998) 1039.
[6] E. Aicart, E. Junquera, J. Pharmaceutical Sci. 88 (1999) 626.
[7] K.A. Connors, Chem. Rev. 97 (1997) 1357.
[8] V.T. Yilmaz, A. Karadag, H. Içbudak, Thermochim. Acta 261 (1995) 107.
[9] H.-J. Schneider, F. Hacket, V. Rüdiger, H. Ikeda, Chem. Rev. 98 (1998) 1755.
[10] E. Aicart, F. Mendicuti, E. Junquera, Langmuir 15 (1999) 4472.
[11] E. Aicart, E. Junquera, Int. J. Pharm. 176 (1999) 169.
[12] M.T.B Luiz, R. Fett, PI 9802189-9 (1998), A 2309/127.
[13] M.T.B. Luiz, R. Fett, M.M. Meier, Deisy A. Drunkler, B. Szpoganicz, 2001, in press.
[14] I.G. Abo-Elnaga, A.S. El-Dahan, S.H. Rikha, Nahrung 29 (1985) 241.
[15] R. Jenness, J. Dairy Sci. 63 (1980) 1605.
[16] R.E. Verrall, L.D. Wilson, S.R. Siddall, Can. J. Chem. 75 (1997) 927.
[17] A.R. Hedges, Chem. Rev. 98 (1998) 2035.
[18] J.-H. Li, N. Zhang, X.-T. Li, J.-Y. Wang, S.-J. Tian, J. Thermal Anal. 49 (1997) 1527.
[19] F. Trotta, M. Zanetti, G. Camino, Polymer Degradation Stability 69 (2000) 373.