

Thermal decomposition of cyclodextrins (α -, β -, γ -, and modified β -CyD) and of metal-(β -CyD) complexes in the solid phase

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Abstract

The thermal decomposition of solid cyclodextrins (CyDs) (natural CyDs are α -, β -, and γ -CyD; modified β -CyDs are triacetyl- (TA-), triphenylcarbamoyl- (TC-), and dimethyl- β -CyD (DM- β -CyD)) and of metal- β -CyD complexes (metal = Ca, Zn, Cd) has been studied by thermal analysis under the same conditions (heating rate = 10 deg min⁻¹; in He). Most of the water molecules are released below 100°C in natural CyDs. Other strongly bound (included) water molecules were found in both α -CyD and γ -CyD, from which the water molecules were liberated at 260–270°C. The decomposition temperature of the CyD ring is lowered in β -CyD because this ring is of lowest symmetry among the three natural CyDs. Although no difference could be found between the 50%-decomposition temperatures of the CyD rings, the final decomposition rate (up to 550°C) distinguished between α -CyD and γ -CyD (both 98%), and β -CyD (86%). The water contents of the modified β -CyDs are much smaller than the natural β -CyD, and TC- β -CyD has only included water molecules. The decomposition temperature of the CyD ring after dehydration, both in TA- and DM- β -CyD is higher by 20–60°C than that of the parent β -CyD. The thermal stability of modified β -CyDs increased in the order TC- < DM- < TA- β -CyD.

Metal- β -CyD complexes have been isolated. All complexes contain water molecules, but these are not tightly bound. Ethanol, which was used as a precipitation reagent, was included only in the Cd- β -CyD complex. Complexation of a heavy metal ion to β -CyD leads to a depression of the thermal degradation of the β -CyD ring.

INTRODUCTION

Recently, cyclodextrins (CyDs) have been applied to bioavailable materials such as drugs and bioindustrial products, because of their

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capability of forming an inclusion complex with a variety of molecules, and of their non-toxicity [1–4]. CyDs have also been studied as enzyme models [5, 6] and as catalysts in selective syntheses of organic compounds [7, 8]. To achieve the above functions, the chemical modification of CyDs has been extensively studied in order to improve their stability, solubility and dissolution rate, etc.

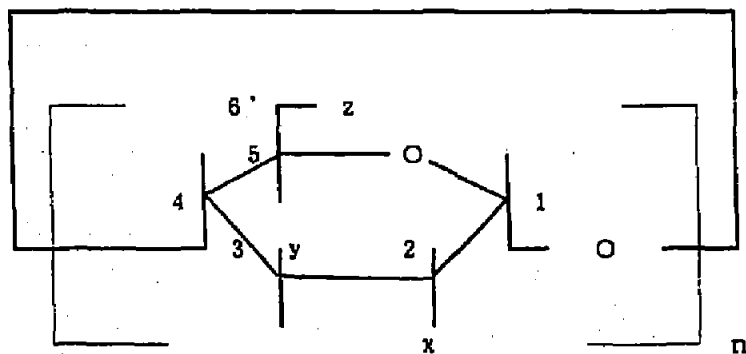
CyDs also act as ligands for metal cations (M), despite the OH groups in CyDs having poor ability to coordinate to M. For example, α - and β -CyD have been known to form Cu(II) complexes with a 2:1 molar ratio of M: CyD [9].

To demonstrate the formation of an inclusion complex with CyD, thermal analysis has often been used [3, 5, 11–14]. Unfortunately, in most cases derivatograms have been interpreted only from a qualitative point of view [10–13, 15] (with some exceptions [14, 16]). In this paper, we describe the thermal decomposition of solid CyD compounds (i.e. natural CyDs (α -, β -, and γ -CyD), chemically modified β -CyDs (see Table 1), and metal- β -CyD complexes) by the use of thermal analysis under the same experimental conditions. From this work, information concerning the relative thermal stabilities of CyDs and their metal complexes has been obtained.

TABLE 1

Cyclodextrin derivatives

Cyclodextrin		Glucose unit (<i>n</i>)	-x	-y	-z
Natural	α -CyD	6	-OH	-OH	-OH
	β -CyD	7	-OH	-OH	-OH
	γ -CyD	8	-OH	-OH	-OH
Chemically modified	DM- β -CyD	7	-OMe	-OH	-OMe
	TA- β -CyD	7	-OAc	-OAc	-OAc
	TC- β -CyD	7	-OCONHPh	-OCONHPh	-OCONHPh



EXPERIMENTAL

Materials

Natural cyclodextrins (α -, β -, γ -CyD) (Nihon Shokuhin Kako Co., Tokyo) were recrystallized from aqueous solution. Two chemically modified β -CyDs were synthesized according to the literature (i.e. heptakis(2,3,6-tri-*O*-acetyl)- β -cyclodextrin (TA- β -CyD) [17] and heptakis[2,3,6-tri-*O*-(*N*-phenylcarbonyl)]- β -cyclodextrin (TC- β -CyD) [18]).

Heptakis(2,6-di-*O*-methyl)- β -cyclodextrin (DM- β -CyD) (Thoshin Chemical Co., Tokyo) was recrystallized from aqueous solution. Their compositions determined by elemental analysis (C, H) and thermal analysis (water content) are given in Table 2. Chemical modifications were also checked by IR spectra.

Thus inclusion complexes M- β -CyD (M = Ca, Cd, or Zn) were prepared by adding the respective metal solution (Ca(OH)₂, CdSO₄, or Zn(NO₃)₂ dissolved in pure water) to aqueous β -CyD solution with stirring, adjusting the pH to 12.5 with NaOH solution. The product precipitated by ethanol was washed with water and ethanol then dried under reduced pressure. The

TABLE 2

Analytical data

CyD or M-CyD	Found (Calc.) (wt.%)				Found (Calc.) (wt.%) Water ^a by TG
	C	H	N	Metal	
α -CyD · 7H ₂ O	39.42, 6.83 (39.34, 6.80)				11.4 (11.5)
β -CyD · 11H ₂ O	37.88, 6.31 (37.84, 6.96)				15.2 (14.9)
γ -CyD · 8H ₂ O	39.80, 6.34 (40.00, 6.73)				9.7 (10.0)
DM- β -CyD · 1.5H ₂ O	49.87, 7.33 (49.52, 7.49)				2.0 (2.1)
TA- β -CyD · 2.5H ₂ O	49.26, 5.56 (48.91, 5.87)				2.9 (2.2)
TC- β -CyD · 4H ₂ O	61.63, 4.72, 7.90 (61.21, 4.97, 7.93)				2.1 (1.9)
Ca _{2.5} (β -CyD) · 11H ₂ O	34.18, 5.11 (34.87, 6.21)			6.72 (6.93)	13.8 (13.7)
Cd ₂ (β -CyD) ₂ · 16H ₂ O · 2EtOH	36.40, 5.14 (36.35, 6.39)			– –	10.3, 3.8 ^a (9.9, 3.2)
Zn _{2.5} (β -CyD) · 22H ₂ O	28.87, 4.83 (29.53, 6.56)			10.21 (9.57)	22.7 (23.2)

^a EtOH.

metal ion content was analyzed by the usual chelatometric titration. Complexation was also checked by UV absorption spectroscopy using a Shimadzu UV 260 type spectrophotometer. The analytical experiments were performed under atmospheric humidity (about $45 \pm 10\%$).

Thermal analysis

Thermal analysis was performed on a Rigaku Denki 8113-RH model thermal analyzer (Tokyo) under He atmosphere (about $25 \times 10^{-3} \text{ dm}^3 \text{ min}^{-1}$) at a heating rate of 10 deg min^{-1} . The thermogravimetric analysis (TG) and the differential thermal analysis (DTA) were recorded at the same time. A sample of about 15 mg was packed into a Pt cell and the same amount of Al_2O_3 was used as a reference material for DTA.

Measurement of melting point

Thermal behavior was also directly observed with a Yanako MP 500 micro melting point apparatus under atmospheric pressure.

RESULTS AND DISCUSSION

Thermal behavior of CyD derivatives

DTA curves for the natural CyDs (α -, β -, and γ -CyD) and chemically modified β -CyD derivatives (DM- β -, TA- β -, and TC- β -CyD) are shown in Figs. 1 and 2, respectively.

Dehydration of α -, β -, and γ -CyD $\cdot n\text{H}_2\text{O}$

Dehydration of the α -CyD $\cdot 7\text{H}_2\text{O}$ up to 134°C was 96% (6.7 mol H_2O). Three endothermic peaks were observed at 62, 89, and 105°C , corresponding to 2.3 mol, 1.6 mol and 2.8 mol H_2O , respectively. Dehydration of the γ -CyD $\cdot 8\text{H}_2\text{O}$ up to 130°C was 88% (7 mol H_2O). DTA shows a one-step endotherm in the range 62 – 104°C with a peak at 72°C . In both CyDs, the retained 0.3 mol (α -CyD) and 1 mol (γ -CyD) H_2O were liberated at the high temperatures of 275 and 274°C , respectively, with small endothermic peaks.

In contrast, the dehydration of β -CyD $\cdot 11\text{H}_2\text{O}$ was 100% up to 100°C in one TG stage, although there is a point of inflection at 64°C (corresponding to about 4 mol H_2O): the DTA curve shows this as a small endotherm (30 – 64°C) and as an endothermic peak at $64 \rightarrow 76(\text{max}) \rightarrow 100^\circ\text{C}$. Szafraniek [14] has reported that the entire $11\text{H}_2\text{O}$ in β -CyD are liberated in one

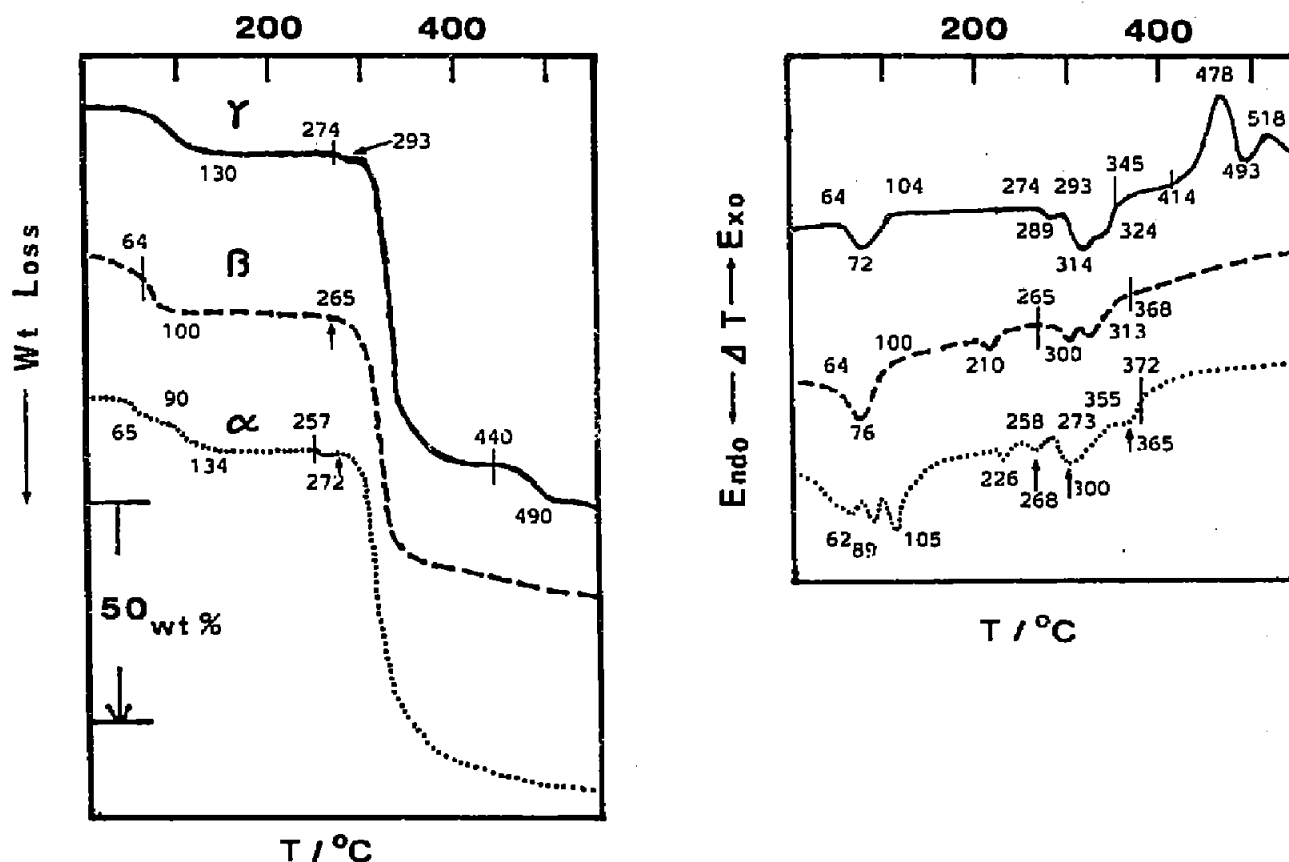


Fig. 1. TG and DTA curves of natural CyDs (α -, β -, and γ -CyD \cdot n H₂O).

stage during thermal decomposition experiments (taking the endothermic peak lying 70–150°C with a heating rate of 8.48 deg min⁻¹). Szafranek has pointed out that the one-step liberation of the entire water content is not consistent with the crystallographic studies that show the 11 water molecules to be shared between the cavity of β -CyD (6.13H₂O) and the external interstices (4.88H₂O) [19, 20].

Thermogravimetric results obtained in our experiments, however, indicate that the latter water molecules escape below 64°C and the former ones escape at 64–100°C. Thus the included water molecules in the β -CyD cavity are considered to be interacting less strongly with the CyD ring. The same consideration apply concerning a part of the above 6.7 (α -CyD) and 7 (γ -CyD) H₂O molecules. The water molecules retained to higher temperatures in α -CyD (0.3 mol) or γ -CyD (1 mol) are thus another type of water molecule, strongly included in the CyD cavity by strong interactions.

Degradation of CyD part of α -, β -, and γ -CyD

Decomposition (after complete dehydration) started from 272 (α -), 265 (β -), and 293°C (γ -CyD). The total weight losses up to 550°C were 98% (α -), 88% (β -), and 98% (γ -CyD). Degradation of α -CyD was

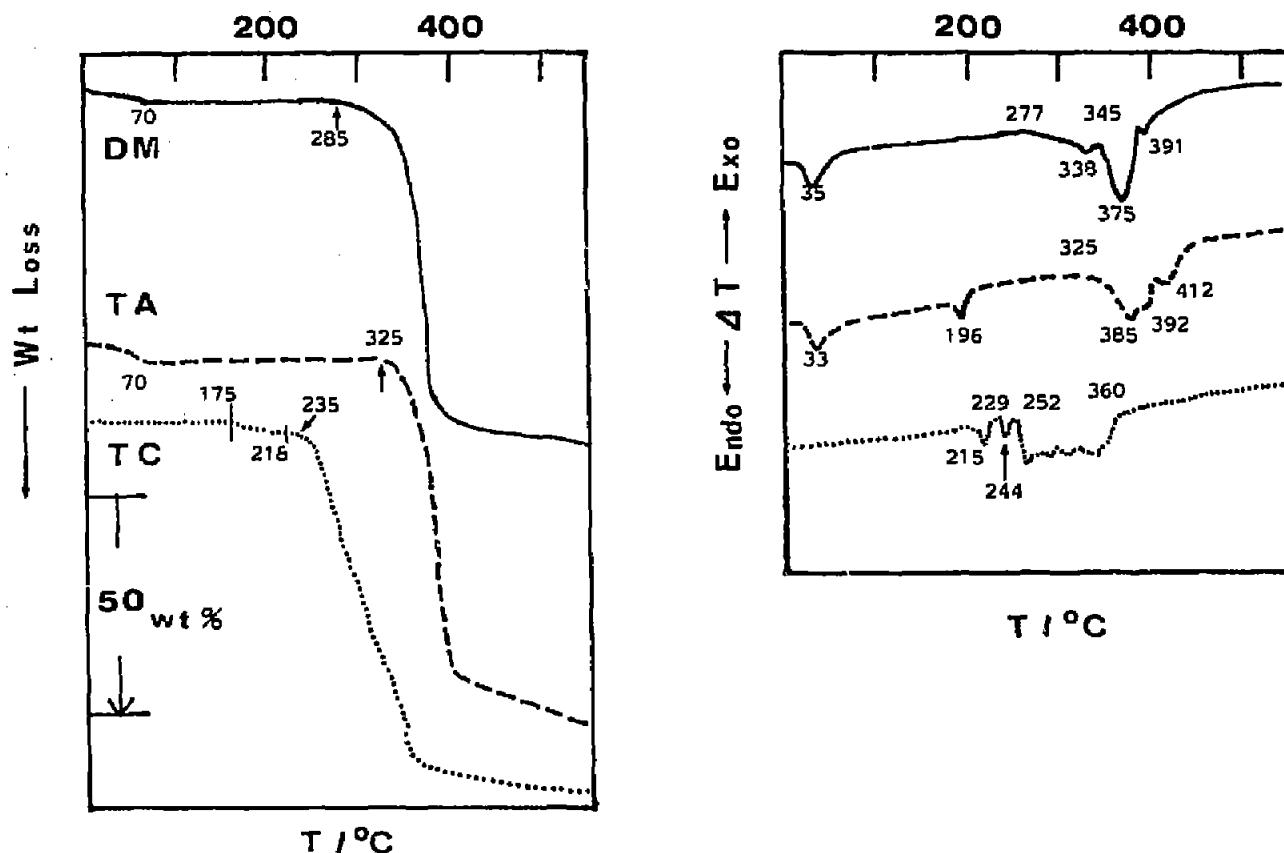


Fig. 2. TG and DTA curves of chemically modified CyDs (DM-, TA-, and TC- β -CyD \cdot n H₂O).

accompanied by broad endothermic peaks in the ranges 273–346°C and 355–372°C, but no significant DTA change was detected above 380°C. Decomposition of β -CyD progressed in the range 265–368°C, with endothermic peaks at 300 and 313°C. The obvious small endothermic change around 210°C without any weight loss is attributed to the transformation of β -CyD [16], for which the peak was observed at 220°C with a heating rate of 5 deg min⁻¹ in air. The same type of peak was observed at 226°C in the case of α -CyD.

On degradation, γ -CyD gave a broad endothermic peak in the range 293–345°C with two peaks at 314 and 322°C. However, behavior characteristic of CyD was observed at a higher temperature range (415–520°C), i.e. a broad exothermic peaks at 478°C and 517°C, with two gradual small weight loss stages.

According to the melting point measurements, melting took place in every CyD (α -, β -, and γ -) in the temp. range 295–315°C. Thus the recorded endothermic changes correspond to melting 273→300°C(max) for α -, 265→300°C(max) for β -, and 293→314°C(max) for γ -CyD, respectively. In every CyD, the evaporation of gaseous products (as very small bubbles) was observed above 320°C. As described above, the

degradation of the α -, β - and γ -CyD parts gave distinct behavior but the 50%-decomposition temperatures of these CyDs are independent of the CyD ring: 322 (α -), 318 (β -) and 324°C (γ -).

Thermal behavior of chemical modified β -CyD \cdot nH₂O

Dehydration process of DM-, TA-, and TC- β -CyD \cdot nH₂O

DM- β -CyD \cdot 1.5H₂O and TA- β -CyD \cdot 2.5H₂O liberated all their water molecules below 100°C. In contrast, dehydration from TC- β -CyD \cdot 5H₂O occurs in two stages: the gradual weight loss below 100°C corresponds to one water molecule, so this endothermic change was not clearly detected. The remaining water molecules (4 mol) were liberated in the higher temperature range of 175–218°C, with a small endothermic peak at 215°C. In this temperature range, melting was taking place simultaneously because the TC- β -CyD has fused at 212–216°C. Among all β -CyD derivatives, this is the only example of water as a guest molecule being included strongly.

When the CyD ring is modified, the water content is decreased below that of the parent β -CyD, although the solubility in water is enhanced. In contrast to the behaviour of the parent β -CyD, no endothermic transformation of CyD around 210°C could be observed in any modified β -CyD.

Decomposition of DM-, TA-, and TC- β -CyD part

After dehydration, DM- β -CyD began to decompose at 285°C and a rapid weight loss continued to 390°C, where three endothermic peaks were detected: a small peak (277 \rightarrow 338°C(max)), a large peak (375°C(max)), and very small peak (391°C(max)). Melting occurred at 305–310°C and continuous evolution of gaseous products was found at 312–335°C. At 335°C the sample became oily, gaseous product was observed again from 370°C, and at the same time the sample became solid. The total weight loss up to 550°C reached 89%. In the case of TA- β -CyD, a small sharp endothermic peak was observed at 196°C without weight loss prior to the degradation of TA- β -CyD part from 325°C.

At the former point the compound is molten. In fact, melting was observed at 198–203°C; the gaseous product was also observed from 270 to 320°C (sample color changed to dark brown). A gradual weight loss continued in the range 325–425°C, with broad (385°C) and small (412°C) endothermic peaks. The overall weight loss up to 550°C was about 93%. After the release of the guest water molecules which were kept tightly within the TC- β -CyD, a continuous degradation (about 90% weight loss) took place at 235–360°C, where the DTA curve gave an unstable endothermic change. The evolution of gaseous product occurred at 230–340°C, where the sample's color changed to dark brown. The total weight loss until 550°C was 96%.

TABLE 3
Thermal stability of CyD ring and tightly included guest molecules based on TG

Parameter	Cyclodextrin										
	β -CyD	α -CyD	γ -CyD	TC- β -CyD	DM- β -CyD	TA- β -CyD	Zn- β -CyD	Ca- β -CyD	Cd- β -CyD		
T_i (°C) ^a	265	272	295	235	285	325	217	245	253		
T_h (°C) ^b	318	322	324	306	371	385	450	320	370		
Melting point (°C) ^c	300	310	300	215	310	196	(300)	300	290		
Guest molecules	-	0.3H ₂ O	1.0H ₂ O	4.0H ₂ O	-	-	-	-	2EtOH		
T_g (°C) ^d	-	257	274	175	-	-	-	-	193		

^a Temperature of initial decomposition of CyD ring part. ^b Temperature of 50%-decomposition of CyD ring part. ^c Temperature of complete melting observed by melting point measurements. ^d Temperature of release of guest molecules.

Comparison of thermal stabilities of CyD derivatives

TG data during the decomposition of the CyD ring is given in Table 3, together with those of the tightly held water molecules. Based on both the temperature of initial decomposition T_i and 50%-decomposition T_h , the order of thermal stability of CyDs has been shown as: TC- β -CyD < β -CyD < α -CyD < DM- β -CyD < γ -CyD < TA- β -CyD. Thus, it was found that β -CyD with a structure of low symmetry has the lowest stability among three natural CyDs (α -, β -, and γ -CyD). In order to improve the stability, chemical modification is found to be effective: converting β -CyD ring into DM- β -CyD or TA- β -CyD.

Thermal behavior of inclusion complexes of metal ion with β -CyD

Formation of inclusion complexes and their compositions

The UV absorption spectra in aqueous solution of $\text{Ca}_{2.5}$ (β -CyD)-type complexes are shown in Fig. 3. Analytical and spectral data of β -CyD complexes with Ca, Cd and Zn are given in Tables 2 and 4, respectively.

A new absorption band at 256 nm has been observed in the Ca inclusion complex (Fig. 3). The Zn inclusion complex gave a shoulder absorption at 259 nm. The shoulder absorption of the Cd complex gave a smaller longer-wavelength shift (224 nm) than that of the parent β -CyD, and the molar extinction coefficient is enhanced 25-fold. The band may contribute

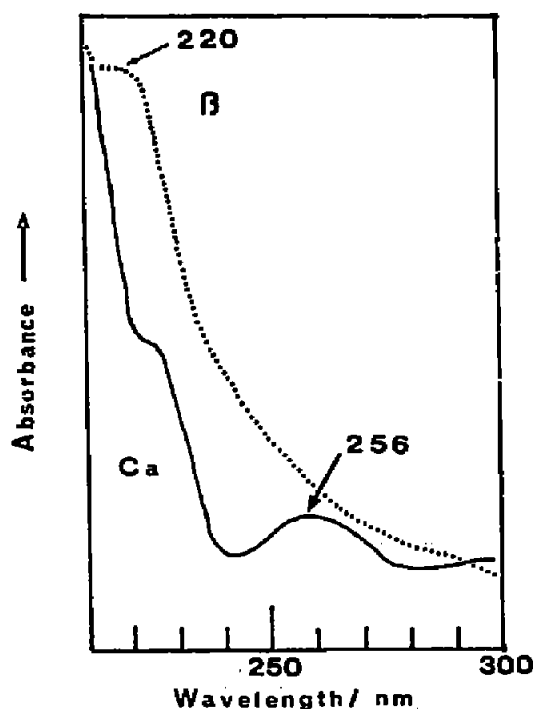


Fig. 3. UV spectra of β -CyD and its Ca complex in aqueous solution.

TABLE 4

The electronic spectral data of M- β -CyD complexes in water solvent

M	λ (nm)	ϵ (cm ⁻¹ mol ⁻¹ dm ³)
Ca	256	760
Cd	224 (sh)	5110
Zn	259 (sh)	1210

Key: sh, shoulder.

to the charge transfer transition from the secondary OH group of CyD to the metal ion.

The above data (Tables 2 and 4) indicate that the composition of the inclusion complexes are $\text{Ca}_{2.5}(\beta\text{-CyD}) \cdot 11\text{H}_2\text{O}$, $\text{Cd}_2(\beta\text{-CyD})_2 \cdot 16\text{H}_2\text{O} \cdot 2\text{EtOH}$, and $\text{Zn}_{2.5}(\beta\text{-CyD}) \cdot 22\text{H}_2\text{O}$.

Release of water and/or ethanol molecules

DTA curves of $\text{M}(\beta\text{-CyD}) \cdot x\text{H}_2\text{O} \cdot y\text{EtOH}$ are given in Fig. 4. $\text{Ca}_{2.5}(\beta\text{-CyD}) \cdot 11\text{H}_2\text{O}$ loses its $11\text{H}_2\text{O}$ in two steps with endothermic peaks at 30 and 80°C. $\text{Cd}_2(\beta\text{-CyD})_2 \cdot 16\text{H}_2\text{O} \cdot 2\text{EtOH}$ loses its $16\text{H}_2\text{O}$ at 28–151°C in

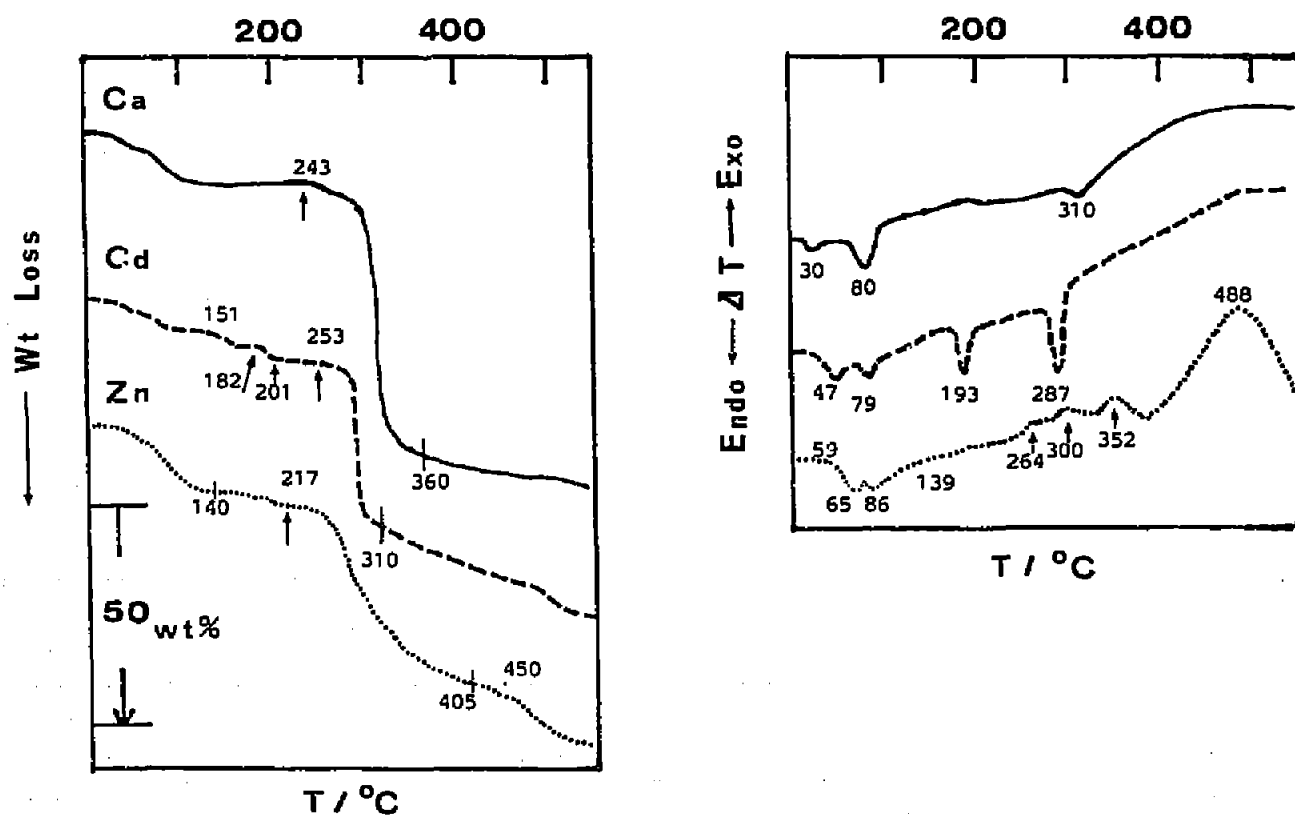


Fig. 4. TG and DTA curves of $\text{Ca}_{2.5}\text{-}\beta\text{-CyD} \cdot 11\text{H}_2\text{O}$, $\text{Cd}_2\text{-(}\beta\text{-CyD)}_2 \cdot 16\text{H}_2\text{O} \cdot 2\text{EtOH}$, and $\text{Zn}_{2.5}\text{-}\beta\text{-CyD} \cdot 22\text{H}_2\text{O}$.

two steps with endothermic peaks at 47°C (7H₂O) and 79°C (9H₂O). The compound loses 2EtOH from 182°C to 201°C, with an endothermic peak at 193°C. The sample powder began to increase its volume from 195°C. Ethanol used as a precipitation reagent is included strongly into the cavities of two CyDs as a guest molecule. Zn_{2.5}(β-CyD) · 22H₂O releases all its 22H₂O in two step at 28–140°C, with a broad endothermic peak at 59–139°C (maximum peaks are at 65 and 86°C). Consequently, the inclusion compounds of divalent heavy metal ions and β-CyD possess many more water molecules than the parent β-CyD.

Decomposition of the CyD ring from the β-CyD complex

Ca_{2.5}(β-CyD) starts to decompose at 243°C and the rapid weight loss continues to 360°C, during which an endothermic change is observed (196 → 310°C(max)). The sample powder becomes a fine powder from 190 to 277°C and the original white color turns to a light brown. Melting is observed at 299–302°C, with a color change to dark brown. The total weight loss up to 500°C is 91%. The decomposition of Cd₂(β-CyD)₂, after the release of the included EtOH, proceeds rapidly from 253 to about 310°C. The sample after volume enhancement (195°C) began to decrease in volume at about 260°C, with a color change to brown. Because DTA gave a sharp endothermic peak at 287°C, the decomposition and melting proceeded simultaneously. In fact, melting is observed at around 290°C. The total weight loss up to 550°C is about 80%. Zn_{2.5}(β-CyD) decomposes in the first weight loss stage from 217 to about 405°C. The total decrease up to 550°C is 82.4%. In contrast to the parent β-CyD, the CyD degradation of the Zn complex proceeds very slowly and during this very small exotherms are observed (three maxima at 264, 300, and 352°C). It is observed that the sample gradually melts around 300°C: melting of the Zn complex is not noticeably different from that of the other metal complexes. The subsequent second weight loss stage over the range 450–550°C is accompanied by an intensive and a broad exothermic peak. By complexation with three kinds of metal ions, the endothermic transformation of β-CyD around 210°C has been removed.

The decomposition temperature of the CyD part of these compounds becomes lower than that of the parent β-CyD: Zn_{2.5}(β-CyD) (217°C) < Ca_{2.5}(β-CyD) (243°C) < Cd₂(β-CyD)₂ (253°C) < β-CyD (265°C). In contrast, the temperature of 50%-decomposition becomes higher: β-CyD (318°C) < Ca_{2.5}(β-CyD) (320°C) < Cd₂(β-CyD)₂ (370°C) < Zn_{2.5}(β-CyD) (450°C). The reason that the inclusion of the heavy metal ions (Cd²⁺ and Zn²⁺) depresses the decomposition of the CyD ring is not clear. However, it is presumably because those ions are strongly coordinated to the O atom of the CyD hydroxyl group, and also the tight fitting of those ions into the cavity through bridging with hydroxide ions. Such interactions have been reported between Cu(II) and β-CyD [9].

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