Carbohydrate Polymers 118 (2015) 36–40

Contents lists available at ScienceDirect

Carbohydrate Polymers

journal homepage: www.elsevier.com/locate/carbpol

Characterization of hydroxypropyl-β-cyclodextrins with different substitution patterns via FTIR, GC–MS, and TG–DTA

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ARTICLE INFO

Article history:
Received 4 October 2014
Received in revised form 17 October 2014
Accepted 24 October 2014
Available online 20 November 2014

Keywords:
Hydroxypropyl-β-cyclodextrin
Degree of substitution
Thermal decomposition
GC–MS
FTIR
TG–DTA

ABSTRACT

The structure and thermal properties of hydroxylpropyl-β-cyclodextrins (HPCDs) with different degrees of substitution (DS) and different substitution sites were evaluated via GC–MS, FTIR, and TG–DTA combined thermoanalytical techniques. The results of GC–MS provided the DS and substitution pattern of the HPCD samples. The IR spectra of HPCDs showed all characteristic peaks corresponding to cyclodextrin. Furthermore, the characteristic peaks for methyl in the hydroxypropyl group at 2960 and 1375 cm^{-1} were observed. The thermal decomposition temperature of HPCDs was about 300 °C to 400 °C and enhanced linearly as the molecular DS increased. The rate of DS rise of HPCDs prepared at a strong alkaline condition was higher than that prepared in a weak alkaline solution.

1. Introduction

Cyclodextrins (CDs) are a family of cyclic oligosaccharides that contain several α-1,4-linked glucopyranose units, which are produced by enzymatic degradation of starch by cyclodextrin–glycosyltransferase (Szejtli, 1998). The three main types of cyclodextrins include α-, β-, and γ-CDs formed by six, seven, and eight glucose units, respectively (Del Valle, 2004). CDs have a specific cylindrical shape with a hydrophilic hydroxyl group on their hydrophilic exterior and a hydrophobic cavity of a specific size (Brewster & Loftsson, 2007). CD incorporates lipophilic compounds inside its cavity by various interactions that in turn increase the solubility, bioavailability, and stability of the guest molecules. Hydroxylpropyl-β-cyclodextrin (HPCD), a hydroxyalkyl derivative of β-CD, is an alternative to native CDs that has improved water solubility and is more toxicologically benign (Gould & Scott, 2005). It was approved by FDA in 1997 as the first approved CD derivative. HPCDs have wide applications in food, pharmaceutics, agriculture, and environmental protection fields (Buschmann & Schollmeyer, 2002; Loftsson & Duchêne, 2007; Morin-Crini & Crini, 2013; Singh, Sharma, & Banerjee, 2002; Szente & Szejtli, 2004).

A variety of processing techniques such as spray drying, fluidized-bed drying, and extrusion are used to produce CD matrices for various applications (Claude & Ubbink, 2006). During processing, amorphous CDs and their complexes are often subjected to significant stresses including shearing and elevated temperatures. The effect of shear is understood well, but much less is known about the influence of thermal decomposition on the properties of CDs.

CDs and substituted β-CDs have been studied to establish the relationship between chemical structure and thermal behavior with particular reference to char yield (Trotta, Zanetti, & Camino, 2000). In 2005, Éhen, Giordano, Sztatisz, Jicsinszky, and Novák investigated α-, β-, γ-CDs and methylated and ethylated β-CD derivatives with TG–MS combined thermoanalytical technique to obtain information about their fragmentation behavior. α-, β-, and γ-CDs marketed by five different companies have been characterized from the thermal and structural point of view by Bettinetti, Novák, and Sorrenti (2002). Studies have reported that the degree of substitution or chemical structure can affect the complex form ability of HPCDs (Buvári-Barcza & Barcza, 1999; Yuan, Jin, & Li, 2008). However, no report about the thermal behavior of HPCDs with different space structures is available.

In the present study, HPCDs with different degrees of substitution and different substitution sites were characterized, and the thermal properties were investigated via TG–DTA combined thermoanalytical technique to determine the effect of chemical structure on the thermal behavior of HPCDs.

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http://dx.doi.org/10.1016/j.carbpol.2014.10.070
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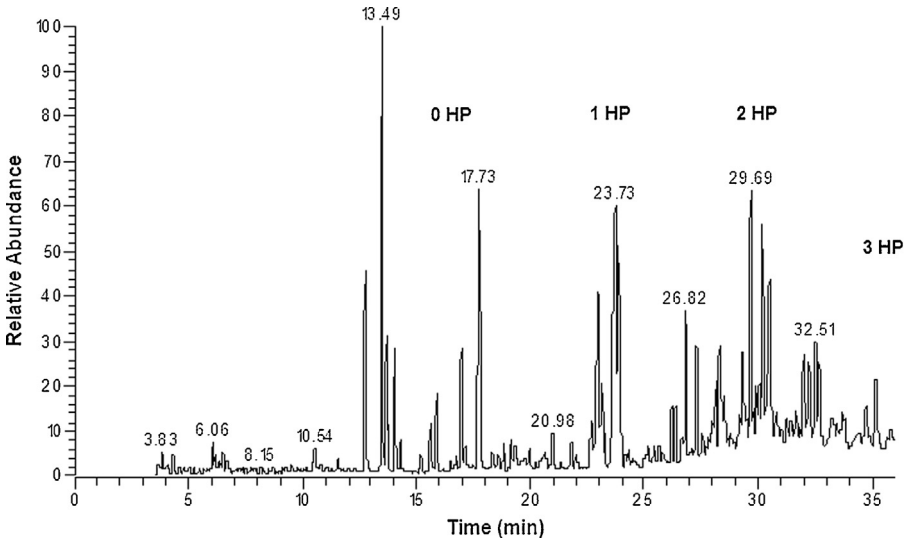

Fig. 1. Total ion current of acetylated D-glucitol ethers.

2. Materials and methods

2.1. Chemicals

HPCD samples were prepared in the laboratory by reacting β-CD with propylene oxide at two different base concentrations [set A (samples 1–3) under 18% and set B (samples 4–6) under 5%], the purity of the HPCDs > 98%. A control (sample 7, 99%) was purchased from Wako Pure Chemical Industries, Ltd. (Chuoku, Osaka, Japan). All other materials were of analytical grade and used without further purification.

2.2. Determination of the substitution pattern and DS of HPCDs

The pretreatment of HPCD samples was performed according to Ciucanu and Kerek (1984). HPCD samples were permethylated, hydrolyzed, and acetylated. The obtained acetylated D-glucitol ethers were detected via GC–MS, which was carried out on a Finnigan Trace MS system with an OV1701 capillary column (30 m × 0.25 mm × 0.25 μm). The carrier gas was helium.

2.3. Fourier transform infrared spectroscopy (FTIR)

The FTIR spectra of the HPCD samples were obtained using a Nicolet 5DXC IR spectrometer (Nicolet, Madison, WI, USA). The procedure consisted of grinding the sample together with KBr (about 200–400 mg) into a fine powder. The powder was then placed into a sampling cup, smoothed, and compressed into the holder by using a compression gauge. The sample was placed in the light path, and the spectrum was obtained from 400 cm^{-1} to 4000 cm^{-1}.

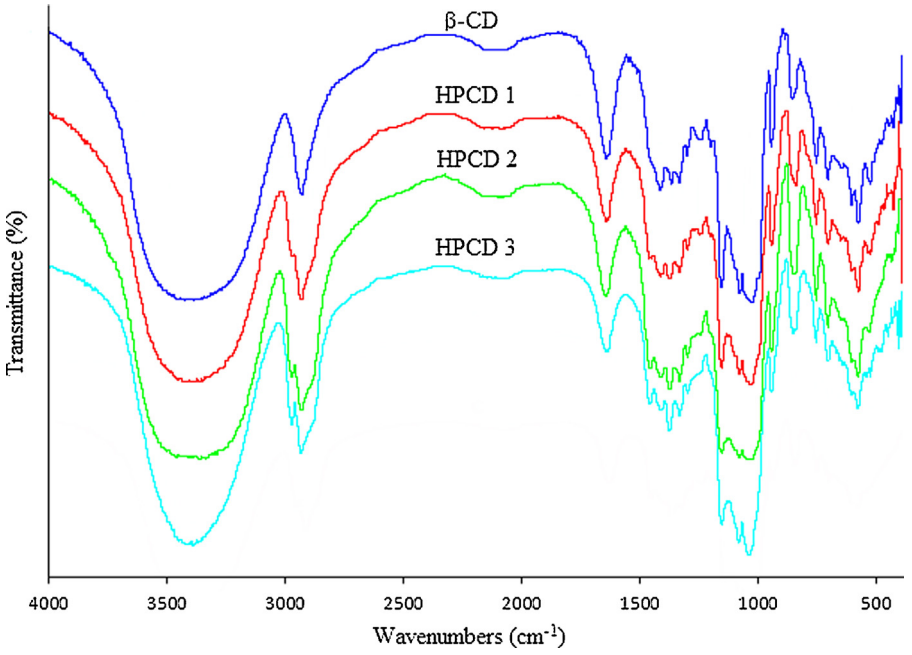

Fig. 2. IR spectra of β-CD and set A HPCDs (samples 1–3).

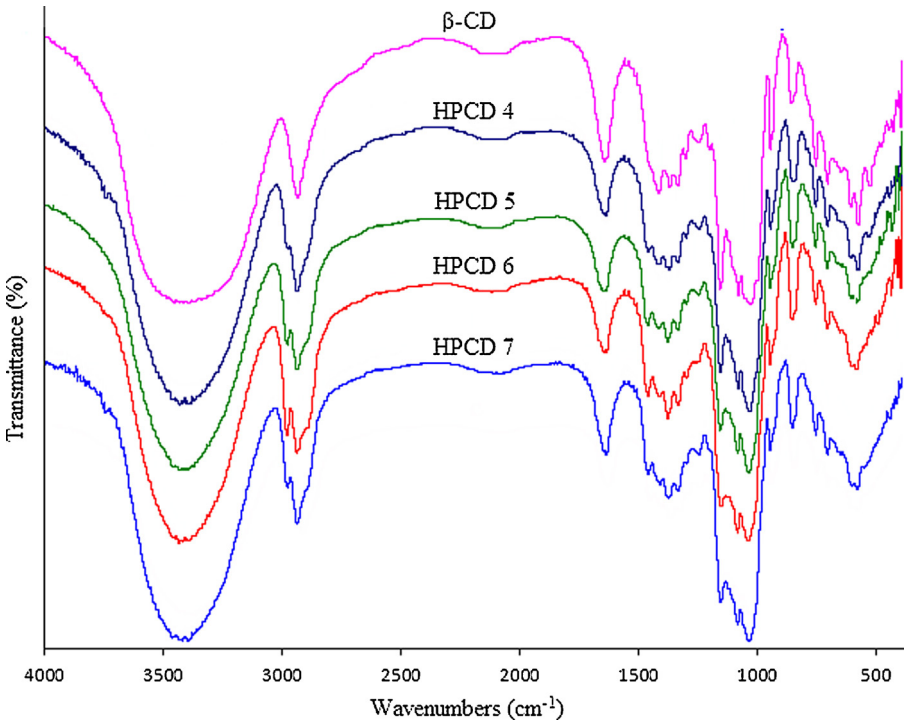

Fig. 3. IR spectra of β-CD, set B HPCDs (samples 4–6) and the control (sample 7).

2.4. Thermogravimetric–differential thermal analysis (TG–DTA)

The TG–DTA system TGA-SDTA 851 (Mettler Toledo, Surich, Switzerland) was adjusted to operate at the following conditions: dynamic atmosphere of helium (99.99%) at 20 mL/min and heating rate of 20 °C/min from 50 °C to 900 °C. The sample mass was about 10 mg.

3. Results and discussion

3.1. Substitution pattern and DS of HPCDs

HPCD molecules decomposed to acetylated D-glucitol ethers after the reductive-cleavage pretreatment. The D-glucitol ethers were separated by a capillary column, and the total ion current of the acetylated D-glucitol ethers of sample 7 is given in Fig. 1. The order of the peaks was according to the number of hydroxylpropyl substituent groups, i.e., more substituent groups took longer retention time. The separated acetylated D-glucitol ethers were then analyzed using a MS system. The fragmentation of the ethers on the electron effect on MS analysis follows established principles. Table 1 shows the configuration information of the HPCD samples. The result shows that the substitution pattern of the hydroxylpropyl substituent group depends on the alkali conditions during preparation, which is in agreement with previous reports (Pitha, Rao, Lindberg, & Seffers, 1990; Yuan & Jin, 2007). In set A, samples were prepared by reacting β-CD with propylene oxide at a strong alkaline condition. The three free hydroxyl groups of glucopyranose units that formed β-CDs were all active at this condition. The DS of O-6 (DS (6)) was the highest, whereas O-2 and O-3 positions also had particular substituents. DS (2 + 3) was approximate to DS (6). The distribution of substituents was homogeneous on the primary (O-6) and secondary hydroxyl groups (O-2 and O-3) of β-CDs. In set B, the HPCD samples were prepared in a weak alkaline solution. The

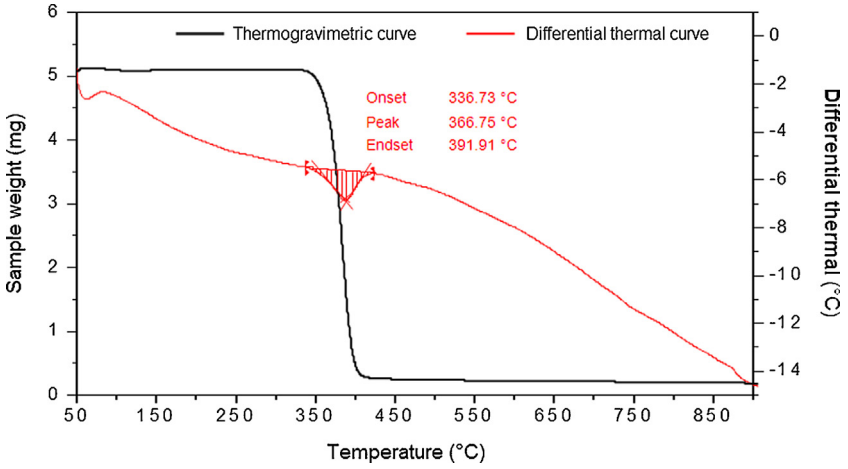

Fig. 4. TG–DTA curves of HPCD (sample 7).

hydroxylpropyl substituents concentrated at O-2. This hydroxyl group was the most active among the three free hydroxyl groups. DS (2 + 3) was about three times of DS (6). Furthermore, the DS value of both sets of HPCD samples increased with the enhancement of the amount of propylene oxide. The difference in substitution sites and DS value may affect the thermodynamic property of HPCDs. After comparing the data, the control (sample 7) was found to be similar with set B samples.

3.2. FTIR spectra studies

The variations in the shape, shift, and intensity of the IR absorption peaks of the samples can provide enough information on the chemical structure transformation. Fig. 2 shows the IR spectra of β-CD and set A HPCDs. The IR spectrum of β-CD showed characteristic bands that are in agreement with a previous report (Ge et al., 2011). The spectra of β-CD and HPCDs both showed characteristic bands belonging to saccharides: 3400 cm^{-1} (O—H stretching vibration), 2930 cm^{-1} (C—H stretching vibration), 1640 cm^{-1} (O—H bending vibration), 1155 cm^{-1} (C—O vibration), and others (Mrozek & Weaver, 2002). A characteristic absorption peak of α-type glycosidic bond was found at 855 cm^{-1}, which indicates that CDs were formed by glucopyranose units through α-1,4-glycosidic bond. The strong absorption peak at 3400 cm^{-1} corresponds to O—H stretching vibration. The absorption was wide and strong because of the decrease in the bond force constant caused by the intramolecular hydrogen bond. The peak of β-CD was wider than that of HPCDs, which indicates that the introduction of hydroxypropyl groups broke the intramolecular hydrogen bond formed between C-2 and C-3. The peak at 2960 cm^{-1} corresponds to the anti-symmetric vibration of methyl groups; β-CD did not have this absorption peak, whereas HPCDs had the peak for the methyl group in hydroxypropyl. The peak proved the existence of hydroxypropyl group. Moreover, the peak area gradually increased from sample 1 to sample 3, which illustrates that the hydroxypropyl substitute group increased in the HPCD molecules and was consistent with the abovementioned DS result. In addition, an absorption peak at about 1375 cm^{-1} for the bending vibration of methyl was found in the IR spectra of HPCDs; it is the characteristic peak of methyl.

Fig. 3 shows the IR spectra of set B and control HPCDs. The peak positions and changes in set B were the same as that in set A samples, and both were the same with the control.

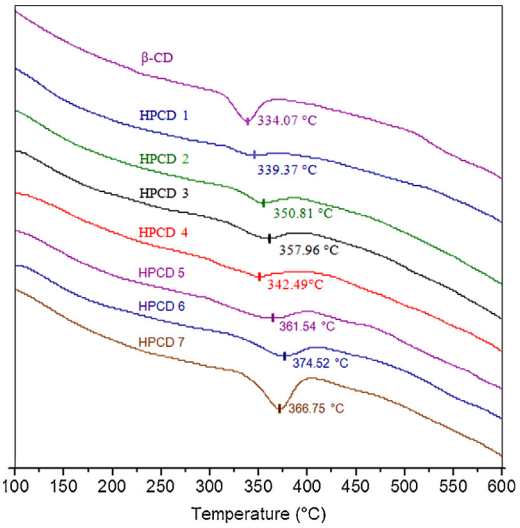

Fig. 5. Differential thermal curve of β-CD and HPCDs.

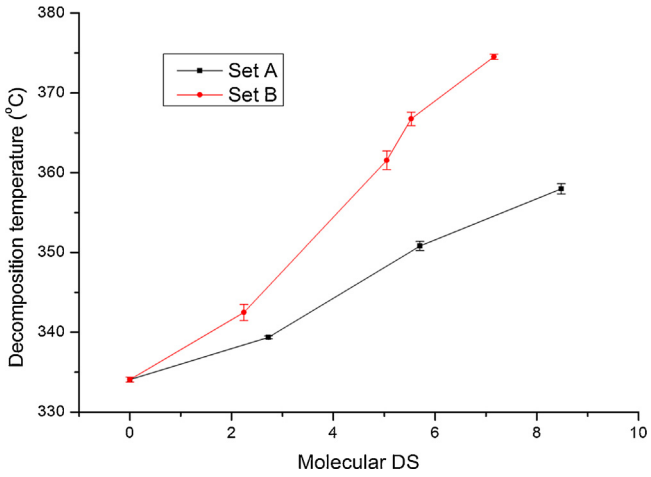

Fig. 6. Correlation plots of thermal decomposition temperature vs. molecular DS of HPCDs. Bars represent the standard deviation for three replicates.

3.3. TG–DTA

The TG–DTA was performed on a TGA-SDTA 851 system. All samples were heated from 50 °C to 900 °C at 20 °C/min heating rate. Based on the TG–DTA results (Fig. 4), no obvious weight loss but only a slight water loss was observed in the thermogravimetric curves at temperature below 300 °C for all the samples. A significant weight loss was observed from 300 °C to 400 °C, and an obvious endothermic peak was found at the corresponding differential thermal curve. The findings indicate that the samples decomposed at this temperature range. The decomposers volatilized and caused the weight loss; meanwhile, the decomposition absorbed heat. At 400 °C, the weight remained approximately constant, which indicates that the samples completed the decomposition. Only high temperature-resistant carbon core remained. The differential thermal curves show only one endothermic peak, which was caused by the temperature difference between the decomposing sample and the furnace. The observation indicates that the thermal decomposition of the samples was a single-step reaction. The TG–DTA results are in agreement with previous reports (Trotta et al., 2000). The endothermic peak was analyzed via graphical differentiation. For sample 7, the onset temperature was 336.73 °C, the ending

Table 1
Distribution of substituents and the respective relative DS value of hydroxyl groups in HPCDs.

Samples	Set A			Set B			
	1	2	3	4	5	6	7
DS (2)	1.02	2.42	3.35	1.15	2.87	3.74	2.85
DS (3)	0.31	0.53	0.76	0.56	1.24	1.87	1.43
DS (6)	1.39	2.75	4.37	0.53	0.94	1.55	1.25
DS (2 + 3)	1.33	2.95	4.11	1.71	4.11	5.61	4.28
DS (2 + 3)/DS (6)	0.96	1.07	0.94	3.23	4.37	3.62	3.42
Molecular DS	2.72	5.70	8.48	2.24	5.05	7.16	5.53
Molecular weight	1293	1466	1627	1265	1428	1550	1456

temperature was 391.91 °C, and the peak temperature was 366.75 °C. The differential thermal curves and peak temperatures of all the HPCD samples are shown in Fig. 5. Fig. 6 shows the changes in thermal decomposition temperature with the molecular DS of HPCDs. The decomposition temperature of HPCDs increased as the molecular DS increased for both set A and set B (sample 7 was included in set B), and the relationship was linear. The result conformed to the rule of thermal decomposition of organic compounds and was similar to several other reports (Kohata, Jyodoi, & Ohyoshi, 1993; Éhen et al., 2005). The increase in covalent bond led to the increase in decomposition temperature. Furthermore, the rate of DS rise in set B was higher than that in set A. Similar to the above GC–MS results on the substitution pattern of HPCDs, the distribution of the substituents was mainly at O-6 in set A HPCDs and at O-2 in set B. The substituents at O-6 were exposed out of the molecules. Hence, set A HPCDs were easier to decompose than set B samples at the same DS. The linear relationship between the thermal decomposition temperature and the molecular DS provides useful information for determining the DS value of the HPCDs by thermal analysis.

4. Conclusions

In this work, the structure of HPCDs was investigated via GC–MS and FTIR analysis, and the thermal properties of HPCDs were studied via TG–DTA. GC–MS was performed to determine the DS value and substitution pattern of HPCDs. For set A HPCDs, which were developed at a strong alkaline condition, the distribution of hydroxypropyl substituents was approximately even, whereas for set B, which were developed at a weak alkaline condition, the hydroxylpropyl substituents concentrated at O-2. The IR spectra showed the existence of hydroxylpropyl substituents, and the result was consistent with the GC–MS result. The thermal decomposition temperature of HPCDs increased linearly as the molecular DS increased. Moreover, the rate of DS rise of set B was higher than that of set A HPCDs. The results may help in determining the DS of HPCDs via thermal analysis.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (grant nos. 31201315 and 31101232).

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