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Thermal decomposition of β-cyclodextrin and its inclusion complex with vitamin E

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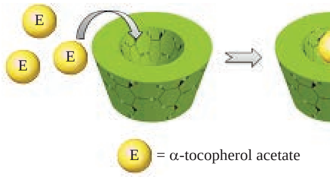
Thermogravimetric kinetic investigation of β-cyclodextrin and its inclusion complex with vitamin E has been carried out. The activation energy and pre-exponential factor of their thermal decomposition have been determined based on the kinetic analysis methods known as the Freeman–Carroll, Sharp–Wentworth, Achar and Coats–Redfern ones.



Keywords: dynamic thermogravimetry, cyclodextrin, pre-exponential factor, thermal analysis, thermal destruction, activation energy.

Advance in the pharmaceuticals design includes a modification of known drug formulations, in particular molecular encapsulation of vitamins through the formation of clathrate-type compounds with α-, β- and γ-cyclodextrins (CDs) as a common method in pharmacology, cosmetology and food industry.[1,2]

CDs represent cyclic oligosaccharides with a lipophilic central cavity and a hydrophilic outer surface.[3] Due to their toroidal structure, CDs are able to form guest–host inclusion complexes with organic compounds[3–5] accompanied with significant changes in the physicochemical properties of the molecules bound to CDs, for example an increase in the stability of guest substances sensitive to the effects of temperature, oxygen or light,[5–7] an elevation of the solubility for poorly-water-soluble substances[8] as well as the transfer of liquid substances into a powder form with masking the disagreeable odors and taste.[9,10] The application of thermal analysis methods like EGA, TGA/DTGA and DSC is important for investigation of the CD complexation with organic substances, including biologically active compounds,[11–14] to assess interactions in their solid dosage forms. In this work, we have explored β-CD and its clathrate complexes with α-tocopherol acetate (vitamin E, VE) using the thermogravimetric kinetic approach.

For the inclusion complexes of VE with β-CD and its (2-octen-1-yl)succinic ester (octenyl-succinic-β-CD), the FT-IR and solid-state NMR spectra have been described.[15] Here we have evaluated the thermal stability as well as dehydration and thermal destruction of the supramolecular β-CD–VE inclusion complexes prepared according to the known procedure[15] with 2 : 1 and 4 : 1 stoichiometry as well as determined the kinetic characteristics of their thermal decomposition, namely the activation energy and pre-exponential factor, using the known methods of Freeman–Carroll,[16] Sharp–Wentworth,[17] Achar[18] and Coats–Redfern[19] (for details, see Online Supplementary Materials).

The thermal properties of encapsulated drugs depend on the type of their interaction with the host[10–12] and are typically manifested in the form of TGA curves. Figure 1 demonstrates the TGA and differential TGA curves obtained in a nitrogen medium for β-CD as well as the two β-CD–VE inclusion complexes at constant heating rate of 10 °C min^{-1}. For all three samples, the mass change proceeds in several steps. The endothermic peak of the release of bound water for the three compounds lies in the range of 50–150 °C, with at least ~90 °C for β-CD and ~110 °C for the inclusion complexes (see Figure 1, horizontal elliptical area).

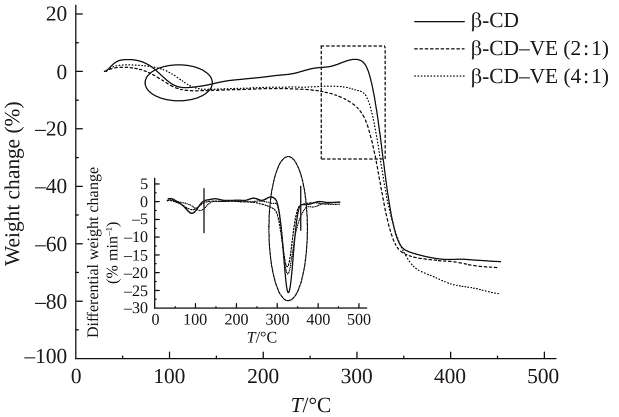


Figure 1 TGA/DTGA curves of β-CD as well as the β-CD–VE inclusion complexes of 2 : 1 and 4 : 1 compositions.

The peak of heat absorption caused by an activation of thermal degradation, namely destruction of glucopyranose units, for β-CD and its inclusion complexes corresponds to the range of 260–360 °C with minima at 310 °C for the 2 : 1complex, 320 °C for the 4 : 1 one and 330 °C for pure β-CD (inset in Figure 1, vertical elliptical area). A small difference in the temperatures of the minima originates from van der Waals forces in the complexes, which are destroyed most quickly with heating, while the β-CD molecule itself begins to break down at higher temperatures. This is confirmed by the shape of mass loss peaks of the complexes (see Figure 1, dashed rectangle area) with shoulders corresponding to a complicated destruction mechanism, initially the complex being destroyed followed by β-CD itself. In general, these data indicate a decrease in the thermal stability of β-CD when VE is incorporated into its cavity.

Kinetic parameters, namely the activation energy E_a and pre-exponential factor A, for the thermo-oxidative destruction process were calculated according to the known procedures[16–19] (for details, see Online Supplementary Materials), the data obtained were collected in Table 1. For the complex of composition 4:1, the activation energy is minimal, *i.e.*, 169.42 kJ mol^{-1} as calculated by the Freeman–Carroll method,[16] and with an increase in the content of VE it grows to 229.12 kJ mol^{-1}, which indicates not only conformational changes in the structure of β-CD, but also an influence of the clathrate structure. From the values of activation energy, we calculated the thermodynamic characteristics, namely the change in Gibbs energy $\Delta G^{\#}$, enthalpy $\Delta H^{\#}$ and activation entropy $\Delta S^{\#}$ (see Table 1). The thermal stability decreased in the order β-CD–VE (4:1) > β-CD–VE (2:1) > β-CD. These results indicate a weak nature of the VE molecules binding to β-CD, *i.e.*, hydrophobic and/or van der Waals type, and can be explained by specific features of formation of the clathrate complex.

The activation energy values calculated by the four independent methods[16–19] have good convergence (see Table 1). However, these methods allowed to obtain the E_a values without knowledge of the pyrolytic mechanism (model) and could not be used to characterize the particular stages of the process, especially taking into account that the E_a values generally depended on the conversion value in a complicated manner. To investigate further the progress of destruction and to estimate the corresponding values of activation energy, we employed the following theoretical mechanism models:[17,20] (i) free nucleation with subsequent growth (A_n), (ii) the order-based equation (F_n) as well as (iii) the contracting sphere model with cylindrical and spherical symmetry (R_n) (for details, see Online Supplementary Materials), the data obtained were collected in Table 2. The highest activation energy values correspond to the order-based model F_n.

The kinetic characteristics obtained for the compounds investigated demonstrated the energy compensation effect, *i.e.*, the linear relationship $\ln A = aE_a + b$,[20] when the theoretical mechanism models A_n and R_n were employed, with an average approximation confidence value $r^2 = 0.90$ (Figure 2). Note that for the more complicated F_n model the graph data were not linear, in this last case it was impossible to use the Coats–Redfern method.

Table 1 Kinetic parameters of thermo-oxidative destruction of β-CD and the β-CD–VE inclusion complexes estimated from TGA/DTGA data.

Compound	Method	E_a/ kJ mol^{-1}	A/s^{-1}	$\Delta G^{\neq}$/ kJ mol^{-1}	$\Delta H^{\neq}$/ kJ mol^{-1}	$\Delta S^{\neq}$/ kJ K^{-1} mol^{-1}
β-CD	ref. 16	548.71	–	133.43	545.01	690.58
	ref. 17	712.24	59.60	129.14	708.54	972.15
	ref. 18	600.84	50.24	129.99	597.14	783.82
	ref. 19	458.70	45.82	130.45	455.00	544.56
β-CD–VE (2:1)	ref. 16	229.12	–	140.03	225.42	141.14
	ref. 17	273.94	22.48	136.07	270.24	221.76
	ref. 18	243.12	19.98	136.67	239.42	169.84
	ref. 19	236.81	27.04	135.14	233.11	161.92
β-CD–VE (4:1)	ref. 16	169.42	–	135.47	165.73	51.64
	ref. 17	244.34	19.59	131.64	240.65	186.02
	ref. 18	190.21	15.17	132.22	186.52	92.67
	ref. 19	185.08	22.29	130.74	181.39	86.43

Table 2 Kinetic parameters of thermo-oxidative destruction of β-CD and the β-CD–VE inclusion complexes estimated from the three theoretical mechanism models.

Compound	Mechanism model[17,20]	E_a/ kJ mol^{-1}	A/s^{-1}	$\Delta G^{\neq}$/ kJ mol^{-1}	$\Delta H^{\neq}$/ kJ mol^{-1}	$\Delta S^{\neq}$/ kJ K^{-1} mol^{-1}
β-CD	A_n	458.70	45.67	130.46	455.00	544.53
	F_n	478.47	47.37	130.28	474.77	578.01
	R_n	440.08	43.85	130.66	436.38	512.95
β-CD–VE (2:1)	A_n	236.81	26.90	130.77	233.12	174.66
	F_n	243.31	27.47	130.67	239.62	185.93
	R_n	230.71	26.14	130.91	227.02	164.01
β-CD–VE (4:1)	A_n	185.08	22.14	136.15	181.38	74.76
	F_n	195.06	23.00	135.96	191.36	91.57
	R_n	175.87	21.13	136.38	172.17	59.15

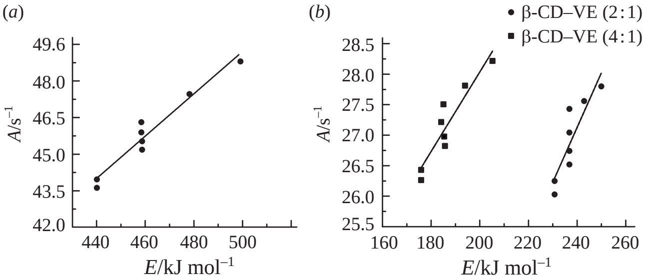


Figure 2 Energy compensation plot for kinetic parameters according to the A_n and R_n mechanism models for (*a*) β-CD and (*b*) β-CD–VE complexes.

In summary, the activation energy and pre-exponential multiplier have been determined for the thermal decomposition of β-CD and its inclusion complexes with VE using the Freeman–Carroll, Sharp–Wentworth, Achar and Coats–Redfern methods with good convergence. The thermal stability decreases in the order β-CD–VE (4:1) > β-CD–VE (2:1) > β-CD, with the corresponding E_a values of 169.42, 229.12 and 548.71 kJ mol^{-1} by the Freeman–Carroll method. Variations in the E_a values calculated by the model-free methods and using the theoretical mechanism models originate from the changes in the process course. The kinetic characteristics obtained demonstrate the energy compensation effect with the free nucleation and contacting sphere mechanisms. The thermal degradation of β-CD and the β-CD–VE complexes begins with removal of water molecules from the β-CD cavity followed by the VE guest, after which the destruction of the cyclic oligosaccharide moieties begins. The results are promising for further understanding the molecular encapsulation of vitamin E compounds.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.01.023.

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