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Thermal decomposition of cholesteryl esters of cynnamic acid derivatives and their effect on the α-tetralylhydroperoxyde free-radical-induced decomposition

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Abstract

Thermal decomposition changes occurring in cholesterol esters of ferulic and sinapic acids were studied by means of TG/DTA. A one-stage decomposition has been established for their thermal degradation in the temperature interval from room temperature to 500°C. The carbon skeleton of the esters determines their thermal stability. By means of TG/DTA studies it has been demonstrated that 4-hydroxy-3-methoxy cholesteryl cinnamate and 4-hydroxy-3,5-dimethoxy cholesteryl cinnamate at content up to 0.0033 mM reduce chain length of tetralin hydroperoxide (0.427 and 0.457 mM) thermal decomposition but inhibition of 'induced' component is not observed. These esters (at content more than 0.008 mM) demonstrated catalytic effect of free radical induced decomposition as a result of reactions generating radicals. 3-Hydroxy-4-methoxy cholesteryl cinnamate (from 0.0089 to 0.0148 mM) suppress tetralin hydroperoxide (0.457 mM) free-radical-induced decomposition.

Keywords: Cholesteryl esters; Cinnamic acid derivatives; Teteralin hydroperoxide; Thermal decomposition

1. Introduction

The esters of natural phenolic acids with triterpenic alcohols and steroids are regarded as food and medicine antioxidants, novel growth promoting vitamins, photoprotectors and effective agents in the treatment of arteriosclerosis [1]. The various physiological functions of these esters evoked our interest in the synthesis of esters of cinnamic acid derivatives with cholesterol [2] and study of their properties [3].

The antioxidant action plays the major role for biological activity of the natural products. The investigations of potential antioxidant properties of newly synthesized compounds in model reactions contribute to clarifying the mechanism of their action. The possibility of application of the synthesized esters as pharmacological substances requires a determination of their thermal parameters. In this work we have studied the thermal decomposition changes occurring with cholesteryl esters of ferulic and sinapic acids by means of TG/DTA from ambient temperature up to 500°C. The effect of cholesteryl esters of four cinnamic acid derivatives (4-hydroxy-3-methoxy cholesteryl cinnamate, 3-hydroxy-4-methoxy cholesteryl

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cinnamate, 4-hydroxy-3,5-dimethoxy cholesteryl cinnamate and 4-hydroxy cholesteryl cinnamate) on the tetralylhydroperoxide free-radical induced decomposition have also been considered. The results obtained are reported in this paper.

2. Experimental

Cholesteryl esters of ferulic (**1**), *iso*-ferulic (**2**), *p*-coumaric (**3**) and sinapic (**4**) acids were synthesized according to the method described in [2].

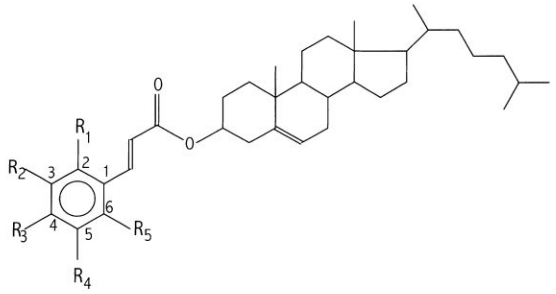
Tetralylhydroperoxide (THPO) was prepared by air oxidation of tetralin [4] and used after a three-fold recristallization from petroleum ether (bp 30–50°C). Its purity was checked by melting point +54.6°C.

The thermal analyses were carried out on Derivatograph Q-1500 (MOM, Budapest) under the following conditions: balance sensivity ±1 mg; Pt crucible with diameter of 7 mm. The TG/DTA experiments were conducted from ambient temperature up to 500°C in a self-generated atmosphere.

3. Results and discussion

The esters **1**, **2**, **3** and **4** (Scheme 1) were investigated by thermal analysis. The data from TG/DTA measurements demonstrate thermal decomposition of 4-hydroxy-3-methoxy cholesteryl cinnamate **1** within the temperature range 245–415°C (Fig. 1, Table 1). The temperature of maximum decomposition rate (W_{max}) is 340°C.

In our previous investigation [5] an intensive thermal decomposition of ferulic acid has been observed in the temperature range of 125–230°C resulting in a 45.7% weight loss. The thermal decomposition of cholesterol (starting material in the syntheses of the



	R_1	R_2	R_3	R_4	R_5
1	H	OCH3	OH	H	H
2	H	OH	OCH3	H	H
3	H	H	OH	H	H
4	H	OCH3	OH	OCH3	H

Scheme 1. Investigated cholesteryl esters of cinnamic acid derivatives.

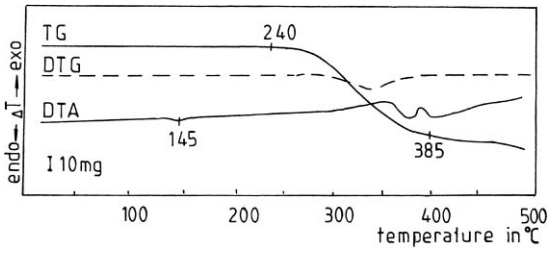


Fig. 1. Thermal decomposition of 4-hydroxy-3-methoxy cholesteryl cinnamate.

Table 1
Thermal decomposition data for 4-hydroxy-3-methoxy cholesteryl cinnamate and 4-hydroxy-3,5-dimethoxy cholesteryl cinnamate

No.	Investigated esters	T_i[a] (°C)	T_f[b] (°C)	$T_{W_{max}}$[c] (°C)	Thermal effects (°C)		Residue (%)
					Endo	Exo	
1.	4-Hydroxy-3-methoxy cholesteryl cinnamate	245	415	340	145, 360, 385	350	11.6
2.	4-Hydroxy-3,5-di-methoxy cholesteryl cinnamate	140	395	340	360, 390	345	15.6

[a] Initial decomposition temperature.
[b] Final decomposition temperature.
[c] Temperature of maximum decomposition rate, from DTG peaks.

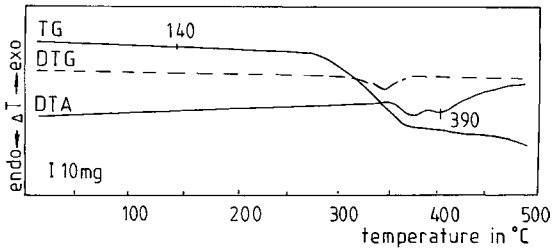


Fig. 2. Thermal decomposition of 4-hydroxy-3,5-dimethoxy cholesteryl cinnamate.

investigated esters) proceeds within the temperature range 245–470°C in a self-generated atmosphere. Alexander et al. [6] registered cholesterol thermal decomposition in nitrogen atmosphere in the temperature range 210–370°C. Endo effects of **1** observed at 360°C and 385°C (Fig. 1) are most probably due to the decomposition of the cholesteryl fragment.

The TG/DTA data demonstrates that 75% of the thermal decomposition of 4-hydroxy-3,5-dimethoxy cholesteryl cinnamate **4** takes place in the temperature range 140–450°C (Fig. 2, Table 1). The temperature of the maximum decomposition rate is 340°C. The DTA curve registers endo effects at 360°C and 390°C (Fig. 2).

It is obvious that the thermal stability of the investigated esters is due to the presence of a cholesteryl fragment in their molecules.

The formed phenoxy radicals from the investigated esters **1**, **2**, **3** and **4** which occur as reactive intermediates in the chain radical reactions are responsible for their antioxidant activity.

In a previous study [5] we established that *p*-hydroxy cinnamic, ferulic and sinapic acid (in specific for each acid concentrations) inhibit the THPO thermal decomposition, carried out in non-isothermal conditions. In raising the acid

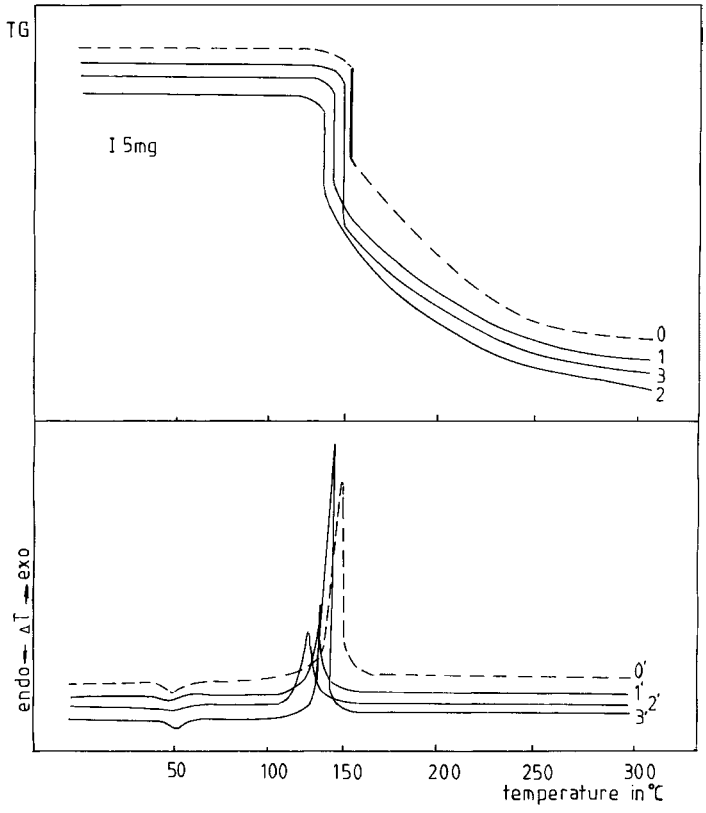
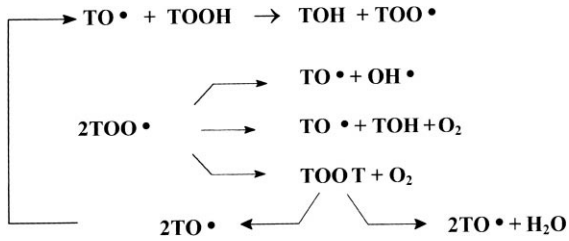


Fig. 3. Thermal decomposition of α-tetralylhydroperoxide in the presence of 4-hydroxy-3-methoxy cholesteryl cinnamate: 0.0′ — 0.427 mM THPO; 1.1′ — 0.427 mM THPO+0.00178 mM 1; 2,2′ — 0.427 mM THPO+0.0035 mM **1**; 3,3′ — 0.427 mM THPO+0.0084 mM **1**.

concentrations in the systems THPO/acid, such effects were not observed. The reactivity of phenoxy radicals in hydrogen abstraction reactions and the thermal decomposition of THPO formed by reaction (1) determine their behavior:

$$PhOH + TO_2^{\bullet} \rightarrow PhO^{\bullet} + TOOH \quad (1)$$

It is known that the phenols have been used to suppress the 'induced' component of hydroperoxide thermal decomposition [7]. In our investigations [8] free-radical-induced decomposition of 0.427 mM THPO without solvent at 165°C has been observed. In the presence of acceptors of free radicals as 2,6-di-*tert*-butyl-4-methyl phenol and phenyl-α-naphthylamine this process is replaced by a purely thermochemical destruction. The radical induced decomposition of THPO can be described by the Scheme 2.



Scheme 2. Free radical induced decomposition of THPO.

In this paper, we investigate the effect of cholesteryl esters on the THPO decomposition under the same conditions [5].

The ability of the investigated compounds to suppress the free-radical-induced reaction is evaluated by the thermoanalytical parameters of the TG-curves at the temperature where $dG/d\tau \rightarrow \infty$. The decrease of weight losses at the temperature of the free-radical-induced reaction is an evidence for reduction of its chain length. TG/DTA data of the reaction systems THPO/4-hydroxy-3-methoxy cholesteryl cinnamate **1** is shown in Fig. 3 and Table 2. A tendency of decrease of the amount of decomposed product was registered from the experiments with 0.427 mM THPO and 0.00178 and 0.0035 mM 4-hydroxy-3-methoxy cholesteryl cinnamate. The weight loss at 135°C during THPO thermal decomposition in the presence of 0.0035 mM of **1** decreases by 6.4% as compared with that of the neat THPO (Fig. 3, curve 2, Table 2). The height of the exothermal peaks at 145°C and 135°C, which corresponds to the thermal effects of interaction

Table 2
Thermal decomposition of α-tetralylhydroperoxide in the presence of compounds **1**, **2**, **3** and **4**

No.	Investigated systems	T_i (°C)	Free-radical-induced decomposition (°C)	Mass loss[a] (%)	T_f (°C)	Thermal effects (°C)	
						Endo	Exo
1.	0.427 mM THPO	105	165	30.0	260	55	150
2.	0.427 mM THPO+0.00178 mM **1**	115	145	29.2	265	55	145
3.	0.427 mM THPO+0.0035 mM **1**	110	135	23.6	270	55	135
4.	0.427 mM THPO+0.0089 mM **1**	110	150	33.5	270	55	150
5.	0.427 mM THPO+0.0178 mM **1**	115	155	46.5	270	55	155
6.	0.427 mM THPO+0.00178 mM **2**	105	145	18.0	290	54	145
7.	0.427 mM THPO+0.0089 mM **2**	110	–	–	315	54	140
8.	0.427 mM THPO+0.0148 mM **2**	115	–	–	330	54	145
9.	0.457 mM THPO	115	160	29.8	260	54	160
10.	0.457 mM THPO+0.0037 mM **3**	110	155	25.9	320	54	155
11.	0.457 mM THPO+0.0094 mM **3**	115	160	23.7	325	54	160
12.	0.457 mM THPO+0.0131 mM **3**	115	160	21.25	325	55	160
13.	0.457 mM THPO+0.00178 mM **4**	105	160	19.8	320	54	160
14.	0.457 mM THPO+0.0033 mM **4**	105	–	–	325	54	145
15.	0.457 mM THPO+0.0084 mM **4**	110	145	42.3	320	54	145
16.	0.457 mM THPO+0.0101 mM **4**	115	Explosive decomposition reaction				

[a] During free-radical-induced decomposition.

between THPO radicals and the compound **1**, significantly decreases in comparison with that of the neat THPO (Fig. 3, compare curves 0′ and 1′, 2′). TG/DTA data demonstrated scavenger properties of the investigated ester **1** (Fig. 3).

A dramatic catalytic effect on THPO free-radical decomposition was observed at content of ester **1** more than 0.008 mM (as it was found in a lot of experiments). The quantity of decomposition products from the investigated system no. 4 (Table 2) increases by 3.5% as compared with that of neat THPO. On the DTA curve of the thermal decomposition of 0.427 mM THPO and 0.0178 mM **1** an intensive exothermic reaction at 155°C is observed (Fig. 3, curves 3 and 3′). Probably reactions with complicated mechanism of generating radicals take place in the systems.

One of the possible explanations of the catalyzed radical reaction is an interaction between THPO and ester **1**:

$$\mathrm{PhOH + TOOH \rightarrow TO^{\bullet} + PhO^{\bullet} + H_2O} \qquad (2)$$

Even the production of small quantities of $TO^{\bullet}$ would lead to initiation of THPO induced decomposition (see Scheme 2).

These results demonstrate radical acceptor properties of ester **1**, but inhibition of THPO induced decomposition is not observed.

The essential difference for the THPO induced decomposition is observed in the presence of 3-hydroxy-4-methoxy cholesteryl cinnamate **2**. Compound **2** inhibits THPO induced decomposition. In the presence of 0.0089 and 0.0148 mM of **2** this process is replaced by a purely thermochemical destruction (Fig. 4, curves 2, 2′ and 3, 3′).

The difference between the effects of compounds **1** and **2** on the THPO free-radical-induced decomposition is more probably due to the different reactivity of OH in their molecules.

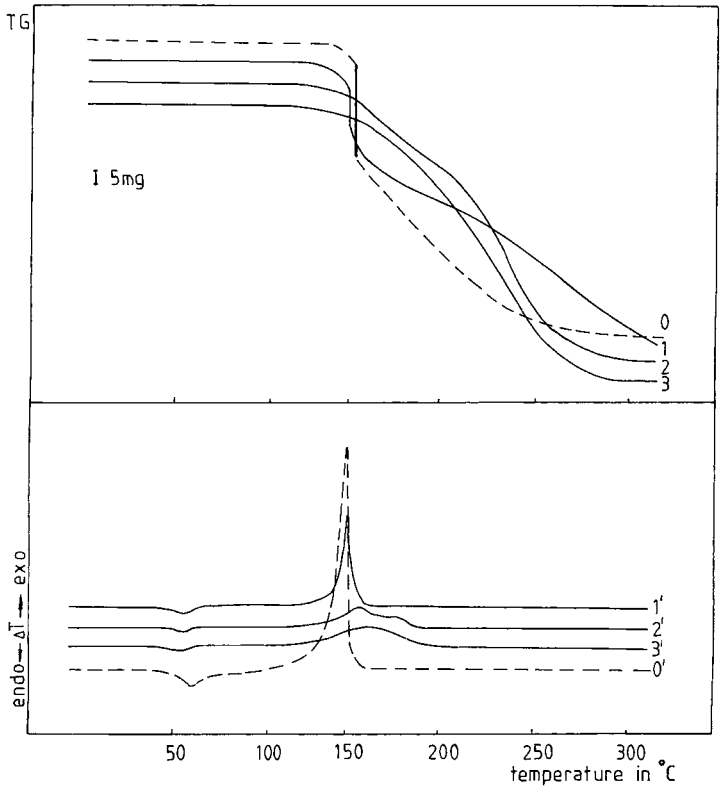


Fig. 4. Thermal decomposition of α-tetralylhydroperoxide in the presence of 3-hydroxy-4-methoxy cholesteryl cinnamate: 0.0′ — 0.427 mM THPO; 1.1′ — 0.427 mM THPO+0.00178 mM 2; 2,2′ — 0.427 mM THPO+0.0089 mM **2**; 3,3′ — 0.427 mM THPO+0.0148 mM **2**.

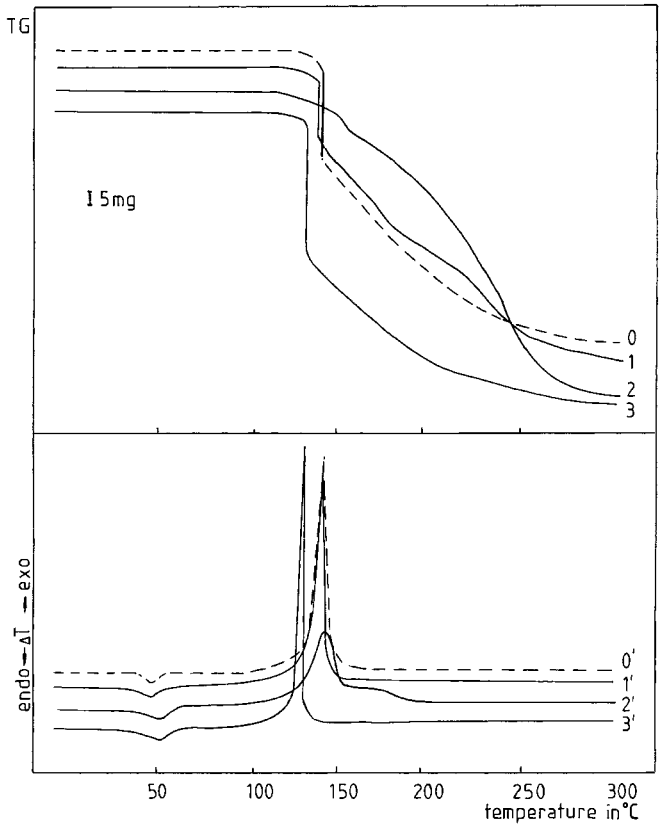


Fig. 5. Thermal decomposition of α-tetralylhydroperoxide in the presence of 4-hydroxy-3,5-dimethoxy cholesteryl cinnamate: 0.0′ — 0.427 mM THPO; 1.1′ — 0.457 mM THPO+0.00178 mM **4**; 2,2′ — 0.457 mM THPO+0.0033 mM **4**; 3,3′ — 0.457 mM THPO+ 0.0084 mM **4**.

To eliminate the effect of the methoxy group on the reactivity of OH we have carried out experiments with 4-hydroxy-cholesteryl cinnamate **3**. The TG data of compound **3** indicates decrease of the weight losses at 140°C (0.0037 mM), 145°C (0.0094 mM) and 150°C (0.013 mM) (Table 2). Compound **3** manifests radical acceptor properties during the THPO free-radical-induced decomposition, the chain length is reduced, but inhibition of this process is not observed.

4-Hydroxy-3,5-dimethoxy cholesteryl cinnamate **4** suppresses THPO induced decomposition in the systems containing 0.457 mM THPO and 0.00178 mM **4** (Fig. 5, curves 1 and 1′), but inhibition effect is observed in the presence of 0.0037 mM ester (Fig. 5, curves 2 and 2′). The free-radical decomposition is replaced by a purely thermochemical destruction. The thermal reaction between THPO and compound **4** results in obtaining of thermally stable molecular products that decompose at higher temperature. An initiation of the radical reaction is demonstrated in the system containing 0.0084 mM and 0.0101 mM compound **4** (Fig. 5, curves 3 and 3′, Table 2).

TG/DTA data of THPO thermal decomposition in the presence of various contents of cholesteryl esters of cinnamic acid derivatives shows specific initiation of free-radical-induced decomposition. This could be due to a reaction between THPO and the investigated esters. Thus, the mechanism of generating radicals in the studied systems is rather complicated.

4. Conclusions

A one-stage decomposition of 4-hydroxy-3-methoxy cholesteryl cinnamate and 4-hydroxy-3,5-dimethoxy cholesteryl cinnamate has been established

during their thermochemical degradation under non-isothermal conditions in the temperature interval from room temperature to 500°C. The carbon skeleton of the esters determined their thermal stability.

4-Hydroxy-3-methoxy cholesteryl cinnamate and 4-hydroxy-3,5-dimethoxy cholesteryl cinnamate at content up to 0.0033 mM reduce the chain length of α-tetralylhydroperoxide thermal decomposition (0.427 and 0.457 mM) but inhibition of 'induced' component is not observed. At content more than 0.008 mM these esters demonstrate catalytic effect on THPO free-radical-induced decomposition as a result of reactions generating radicals.

3-Hydroxy-4-methoxy cholesteryl cinnamate (at content from 0.0089 to 0.0148 mM) suppresses α-tetralylhydroperoxide (0.457 mM) free-radical-induced decomposition.

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