Supplementary Material for

Natural chain-breaking antioxidants and their synthetic analogs as modulators of oxidative stress

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Contents

1. Nonsystematic and systematic names of the studied compounds.

Table S1. All the studied compounds summarized with their names according IUPAC nomenclature, trivial names and their abbreviations:

Abbr.	Nonsystematic/trivial name	IUPAC systematic name
FA	Ferulic Acid	(E)-3-(4-hydroxy-3-methoxyphenyl)prop-2-enoic acid
DFA		(2E,2'E)-3,3'-(6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-diyl)diacrylic acid
CA	Caffeic Acid	(E)-3-(3,4-dihydroxyphenyl)acrylic acid
DCA		(2E,2'E)-3,3'-(5,5',6,6'-tetrahydroxy-[1,1'-biphenyl]-3,3'-diyl)diacrylic acid
Cr	Creosol	2-methoxy-4-methylphenol
DCr		3,3'-dimethoxy-5,5'-dimethyl-[1,1'-biphenyl]-2,2'-diol
Va	Vanillin	4-hydroxy-3-methoxybenzaldehyde
DVa		6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-dicarbaldehyde
Apo	Apocinin	1-(4-hydroxy-3-methoxyphenyl)ethanone
DApo		1,1'-(6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-diyl)diethanone
Eu	Eugenol	2-methoxy-4-prop-2-enylphenol
DEu		5,5'-diallyl-3,3'-dimethoxy-[1,1'-biphenyl]-2,2'-diol
isoEu	iso-Eugenol	2-methoxy-4-[(E)-prop-1-enyl]phenol
DisoEu		3,3'-dimethoxy-5,5'-di((E)-prop-1-en-1-yl)-[1,1'-biphenyl]-2,2'
M1	Dehydrozingerone	(E)-4-(4-hydroxy-3-methoxyphenyl)but-3-en-2-one
D1		(3E,3'E)-4,4'-(6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(but-3-en-2-one)
M2	Zingerone	4-(4-hydroxy-3-methoxyphenyl)butan-2-one
D2		4,4'-(6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(butan-2-one)
M3		(2Z,5E)-ethyl 2-hydroxy-6-(4-hydroxy-3-methoxyphenyl)-4-oxohexa-2,5-dienoate
D3		(2Z,2'Z,5E,5'E)-diethyl 6,6'-(6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(2-hydroxy-4-oxohexa-2,5-dienoate)

M4		(Z)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)hex-4-en-3-one
D4		(1E,4Z)-1-(2',6-dihydroxy-5'-((Z)-5-hydroxy-3-oxohex-4-en-1-yl)-3',5-dimethoxy-[1,1'-biphenyl]-3-yl)-5-hydroxyhexa-1,4-dien-3-one
M5		(Z)-1-hydroxy-5-(4-hydroxy-3-methoxyphenyl)-1-phenylpent-1-en-3-one
D5		(1Z,4E)-5-(2',6-dihydroxy-5'-((Z)-5-hydroxy-3-oxo-5-phenylpent-4-en-1-yl)-3',5-dimethoxy-[1,1'-biphenyl]-3-yl)-1-hydroxy-1-phenylpenta-1,4-dien-3-one
M6		(1E,4Z)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)hexa-1,4-dien-3-one
D6		(1E,1'E,4Z,4'Z)-1,1'-(6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(5-hydroxyhexa-1,4-dien-3-one)
M7		(1E,4Z)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)hepta-1,4-dien-3-one
M8		(1Z,4E)-1-hydroxy-5-(4-hydroxy-3-methoxyphenyl)-1-(p-tolyl)penta-1,4-dien-3-one
D8		(1Z,1'Z)-5,5'-(6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(1-hydroxy-1-(p-tolyl)pent-1-en-3-one)
M9		(1Z,4E)-1-(4-(tert-butyl)phenyl)-1-hydroxy-5-(4-hydroxy-3-methoxyphenyl)penta-1,4-dien-3-one
D9		(1Z,1'Z)-5,5'-(6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(1-(4-(tert-butyl)phenyl)-1-hydroxypent-1-en-3-one)
HCh	Chavicol	(E)-4-(prop-1-en-1-yl)benzene-1,2-diol
DHCh		5,5'-di((E)-prop-1-en-1-yl)-[1,1'-biphenyl]-2,2',3,3'-tetraol
HPh		(E)-4-(3,4-dihydroxyphenyl)but-3-en-2-one
DHPh		(3E,3'E)-4,4'-(5,5',6,6'-tetrahydroxy-[1,1'-biphenyl]-3,3'-diyl)bis(but-3-en-2-one)
HFA		3-(4-hydroxy-3-methoxyphenyl)propanoic acid
DHFA		3,3'-(6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-diyl)dipropanoic acid
HCA		3-(3,4-dihydroxyphenyl)propanoic acid
DHCA		3,3'-(5,5',6,6'-tetrahydroxy-[1,1'-biphenyl]-3,3'-diyl)dipropanoic acid
Curc	Curcumin	(1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione

2. Spectral characterization of the newly synthesized compounds:

2.1. Compounds M4, M6 and M7

(*Z*)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)hex-4-en-3-one **M4**. (85%): mp 38-40°C (lit.[1] 40-41 °C); (β-ketoenol tautomer): ^{1}H-NMR δ 2.03 (s, 3H), 2.55 (t, *J* = 7.7 Hz, 2H), 2.85 (t, *J* = 7.7 Hz, 2H), 3.87 (s, 3H), 5.45 (s, 1H), 6.50 (bs, 1H), 6.64 (dd, *J* = 2.0, 8.2 Hz, Ar, 1H), 6.65 (d, *J* = 2.0 Hz, 1H), 6.80 (d, *J* = 8.2 Hz, 1H); ^{13}C-NMR δ 24.82, 31.26, 41.38, 55.85, 100.01, 110.95, 114.32, 120.79, 132.60, 143.99, 146.41, 191.17, 193.25; Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83; Found: C, 66.13; H, 6.96.

(*Z*)-1-hydroxy-5-(4-hydroxy-3-methoxyphenyl)-1-phenylpent-1-en-3-one **M6**. (64%): mp 142-143°C (lit.[2] 139.8-141.4 °C); (β-ketoenol tautomer): ^{1}H-NMR δ 2.16 (s, 3H), 3.94 (s, 3H), 5.63 (s, 1H), 6.03 (bs, 1H), 6.33 (d, *J*=16 Hz,1H), 6.92 (d, *J*=8.2 Hz,1H), 7.04 (d, *J*=1.9 Hz, 1H), 7.08 (dd, *J*=1.9, 8.2Hz, 1H), 7.55 (d, *J*=16 Hz, 1H); ^{13}C-NMR δ 26.77, 55.91, 100.66, 109.51, 114.82, 120.28, 122.62, 127.63, 140.06, 146.81, 147.52, 177.96, 196.66; Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02; Found: C, 66.63; H, 6.16.

(1*E*,4*Z*)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)hepta-1,4-dien-3-one **M7**. (58%): mp 141-143°C; (β-ketoenol tautomer): ^{1}H-NMR δ 1.18 (t, *J*=7.5 Hz, 3H), 2.42 (q, *J*=7.5 Hz, 2H), 3.95 (s, 3H), 5.64 (s, 1H), 5.86 (bs, 1H), 6.34 (d, *J*=16 Hz,1H), 6.92 (d, *J*=8.2 Hz,1H), 7.03 (d, *J*=1.9 Hz, 1H), 7.09 (dd, *J*=1.9 Hz, 8.2Hz, 1H), 7.52 (d, *J*=16 Hz, 1H); ^{13}C-NMR δ 9.44, 33.23, 55.96, 99.56, 109.48, 114.81, 120.50, 122.62, 127.77, 139.73, 146.78, 147.66, 177.70, 200.00; Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50; Found: C, 67.75; H, 6.56.

2.2. Compounds D4 and D6

(1*E*,4*Z*)-1-(2',6-dihydroxy-5'-((Z)-5-hydroxy-3-oxohex-4-en-1-yl)-3',5-dimethoxy-[1,1'-biphenyl]-3-yl)-5-hydroxyhexa-1,4-dien-3-one **D4** (65%): mp 66-67 °C; (β-ketoenol tautomer): ^{1}H-NMR δ 2.03 (s, 6H), 2.59 (t, *J* = 7.2 Hz, 4H), 2.85 (t, *J* = 7.2 Hz, 4H), 3.89 (s, 6H), 5.48 (s, 2H), 6.10 (bs, 2H), 6.64 (s, 2H), 6.73 (s, 2H); ^{13}C-NMR δ 24.82, 31.36, 40.29, 56.09, 100.14, 110.55, 122.81, 124.45, 132.59, 141.01, 147.24, 191.14, 193.23; Anal. Calcd. for $C_{26}H_{30}O_8$: C, 66.37; H, 6.43; Found: C, 66.33; H, 6.45.

(1*E*,1'*E*,4*Z*,4'*Z*)-1,1'-(6,6'-dihydroxy-5,5'-dimethoxy-[1,1'-biphenyl]-3,3'-diyl)bis(5-hydroxyhexa-1,4-dien-3-one) **D6** (64%): mp 170-171 °C; (β-ketoenol tautomer): ^{1}H-NMR (DMSO d_6) δ 2.09 (s, 6H), 3.87 (s, 6H), 5.82 (s, 2H), 6.63 (d, *J*=15.6 Hz,2H), 7.07 (d, *J*=2 Hz, 2H), 7.30 (d, *J*=2 Hz, 2H), 7.49 (d, *J*=15.6 Hz, 2H), 9.10 (bs, 2H); ^{13}C-NMR δ (DMSO d_6) 26.91, 56.47, 100.99, 110.28, 120.30, 125.23, 125.82, 125.89, 140.73, 147.00, 148.31, 148.36, 178.62; Anal. Calcd. for $C_{26}H_{26}O_8$: C, 66.94; H, 5.62; Found: C, 66.99; H, 6.66.

2.3. Compounds DisoEu, DHCh, DCA and DHCA

*3,3'-dimethoxy-5,5'-di((E)-prop-1-en-1-yl)-[1,1'-biphenyl]-2,2'-**DisoEu***

^{1}H-NMR δ (acetone d_6) 1.85 (dd, *J*=1.6. Hz, 6.8 Hz, 6H), 3.93 (s, 6H), 5.62 (bs, OH), 6.10-6.18 (series of m, 2H), 6.34 (d, *J*=1.6. Hz, 2H), 6.85 (d, *J*=2.0 Hz, 2H), 7.01 (d, *J*=2.0 Hz, 2H); ^{13}C-NMR δ (acetone d_6) 18.38, 56.03, 107.46, 121.56, 122.38, 125.23, 129.36, 131.12, 143.26, 147.84. Anal. Calcd. for $C_{20}H_{22}O_4$ C, 73.60; H, 6.79; Found: C, 73.65; H, 6.83.

5,5′-diallyl-[1,1′-biphenyl]-2,2′,3,3′-tetraol ***DHCh***

^{1}H-NMR δ (acetone d_6) 3.31 (d, *J*=1.6. Hz, 4H), 5.04 (m, 2H), 5.93 (m, 4H), 6.71 (d, *J*=2.0. Hz, 2H), 6.78 (d, *J*=2.0. Hz, 2H), 7.87 (bs, 2 OH), 8.03 (bs, 2 OH), ^{13}C-NMR δ (acetone d_6) 39.41, 114.45, 114.72, 121.72, 126.52, 132.46, 138.15, 139.75, 145.83. Anal. Calcd. for $C_{18}H_{18}O_4$ C, 72.47; H, 6.08; Found: C, 72.51; H, 6.11.

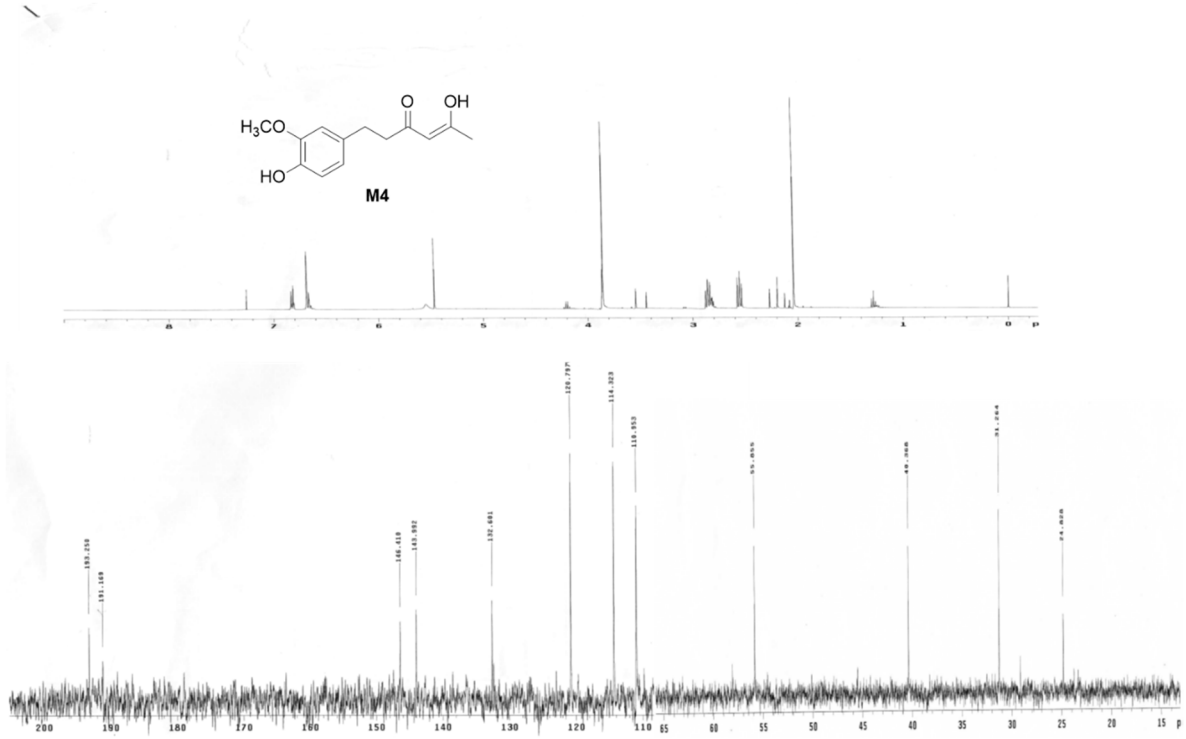
(2E,2′E)-3,3′-(5,5′,6,6′-tetrahydroxy-[1,1′-biphenyl]-3,3′-diyl)diacrylic acid ***DCA***

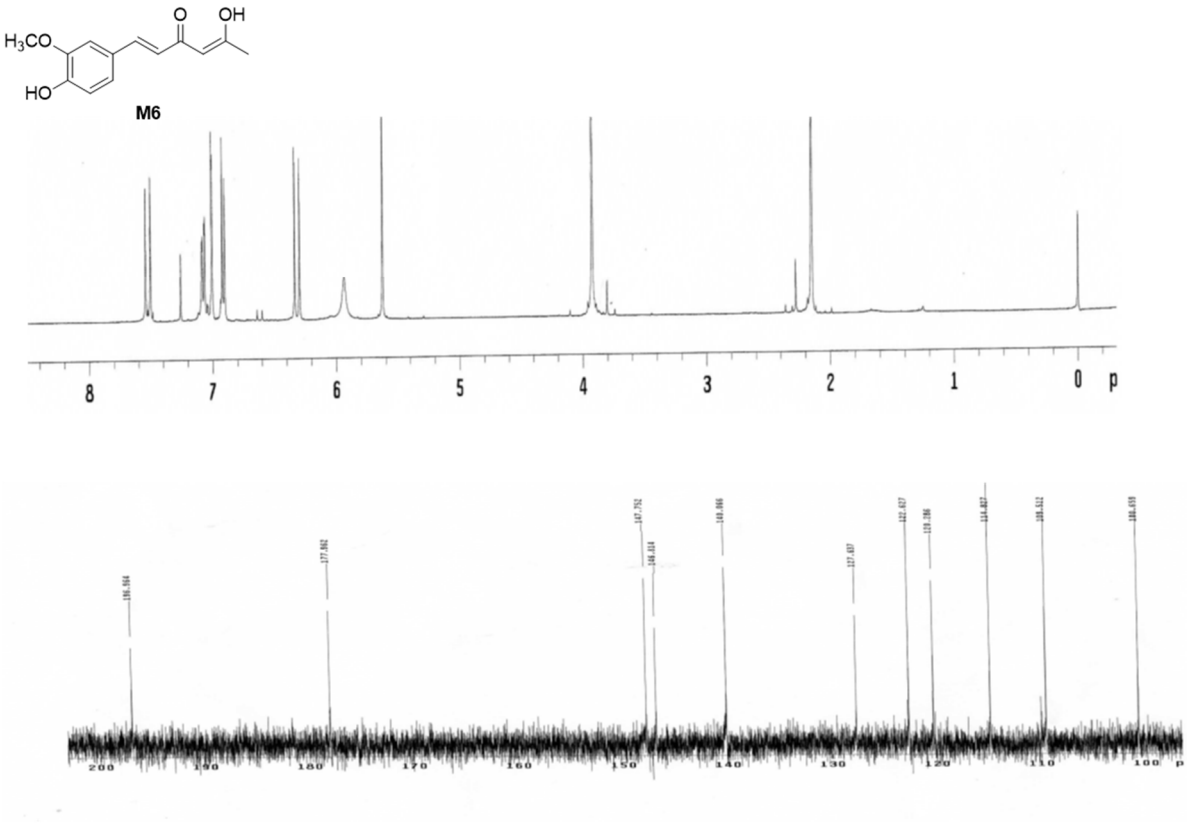
^{1}H-NMR δ (DMSO d_6) 6.15 (d, *J*=16.0 Hz, 2H), 6.89 (d, *J*=2.0 Hz, 2H), 7.02 (d, *J*=2.0 Hz, 2H), 7.41 (d, *J*=16.0 Hz, 2H); ^{13}C-NMR δ (DMSO d_6) 113.08, 115.66, 123.98, 125.22, 126.32, 145.16, 145.97, 146.25, 168.40. Anal. Calcd. for $C_{18}H_{14}O_8$ C, 60.34; H, 3.94; Found: C, 60.44; H, 3.98

3,3′-(5,5′,6,6′-tetrahydroxy-[1,1′-biphenyl]-3,3′-diyl)dipropanoic acid ***DHCA***

^{1}H NMR δ (MeOH d_4) 2.24 (t, *J*=7.2 Hz, 4H), 2.61 (t, *J*=7.2 Hz, 4H), 6.34 (d, *J*=2.0. Hz, 2H), 6.57 (d, *J*=2.0. Hz, 2H);^{13}C-NMR δ (MeOH d_4) 23.90, 31.97, 110.57, 119.38, 127.34, 128.53, 147.48, 174.46, 216. 65. Anal. Calcd. for $C_{18}H_{18}O_8$ C, C, 59.67; H, 5.01; Found: C, C, 59.71; H, 5.21.

2.4. ^{1}H and ^{13}C NMR spectra





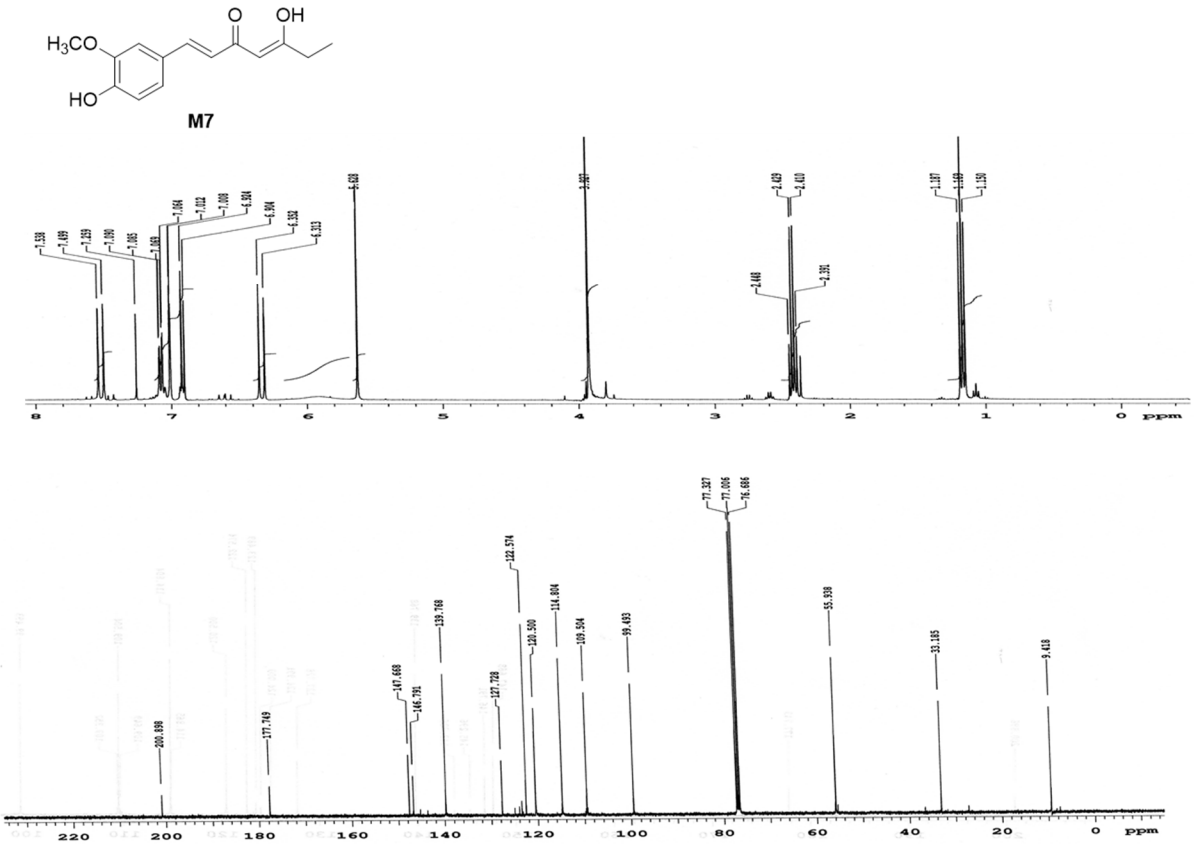
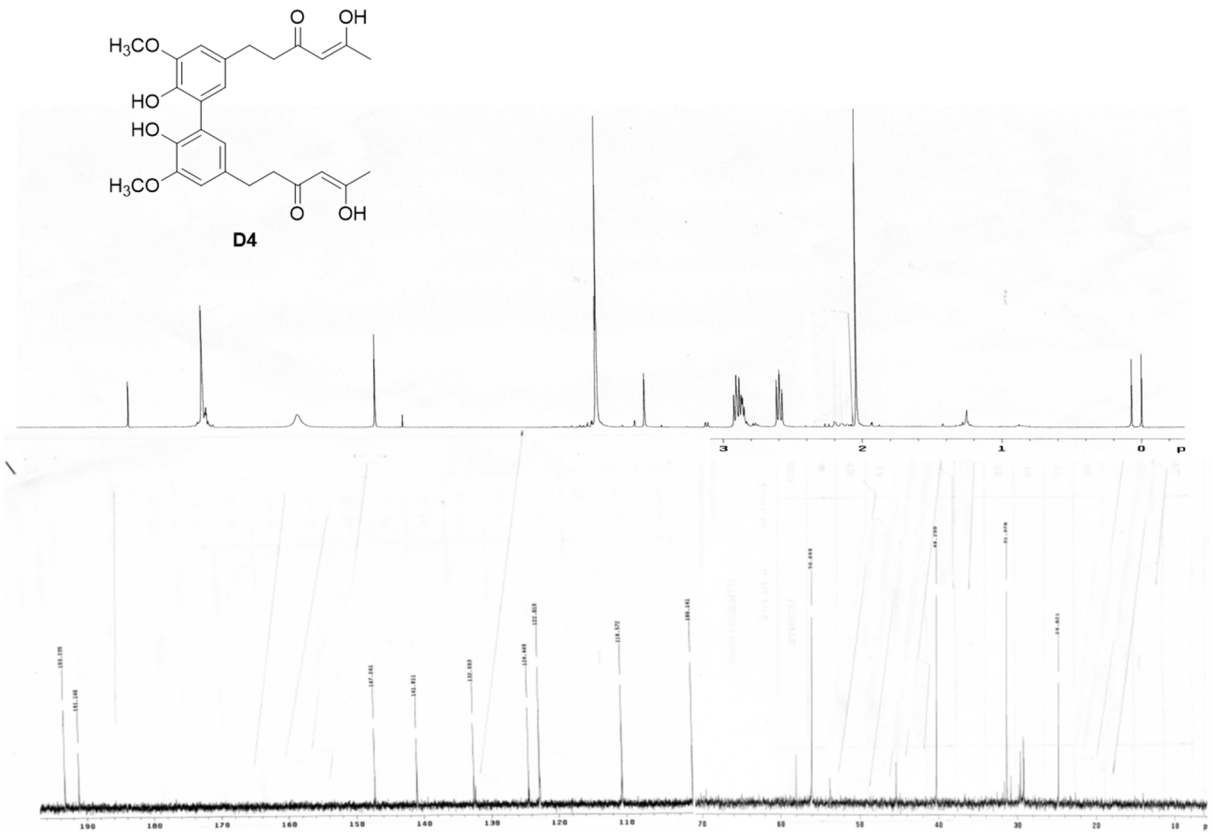


Figure S1. ^{1}H and ^{13}C NMR spectra of **M4**, **M6** and **M7**.



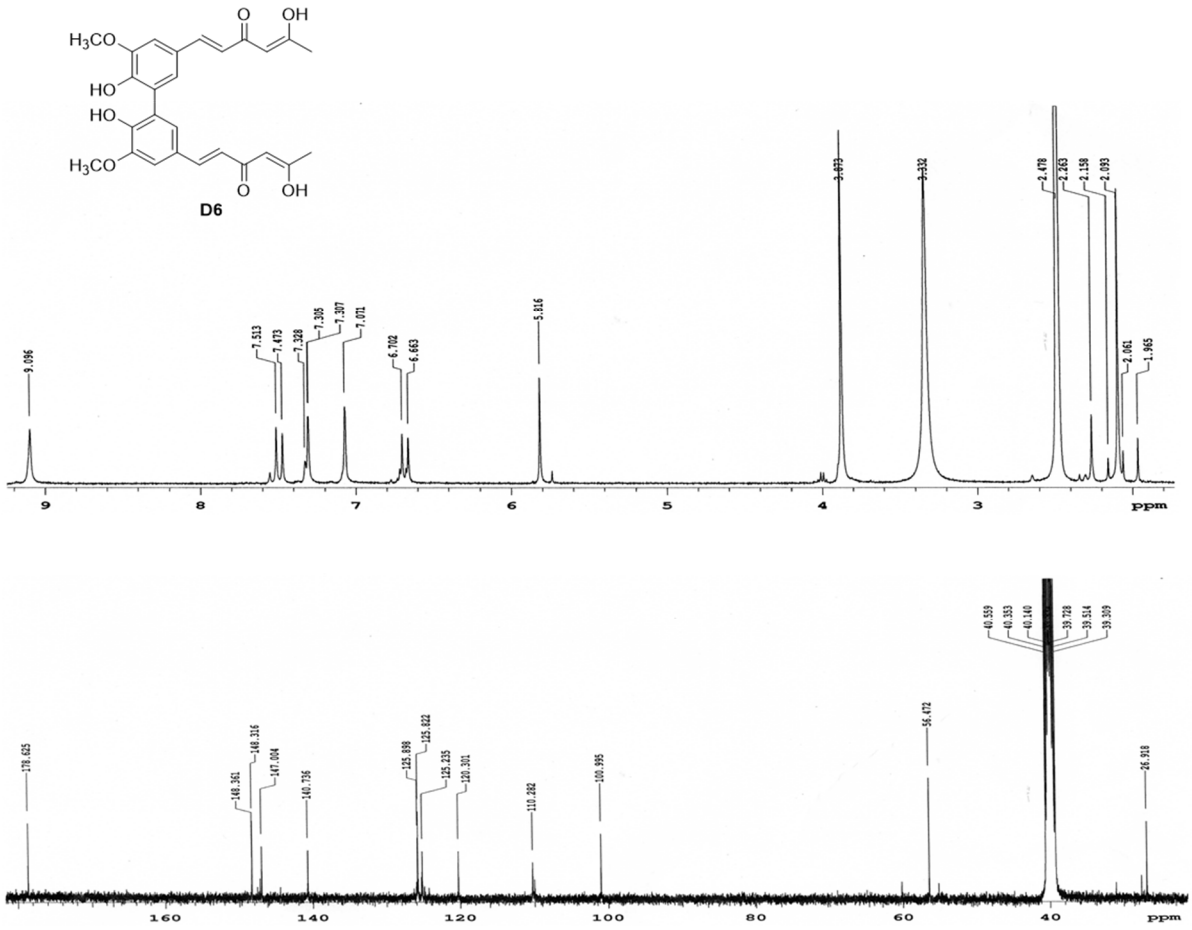
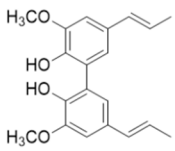


Figure S2. ^{1}H and ^{13}C NMR spectra of **D4** and **D6**.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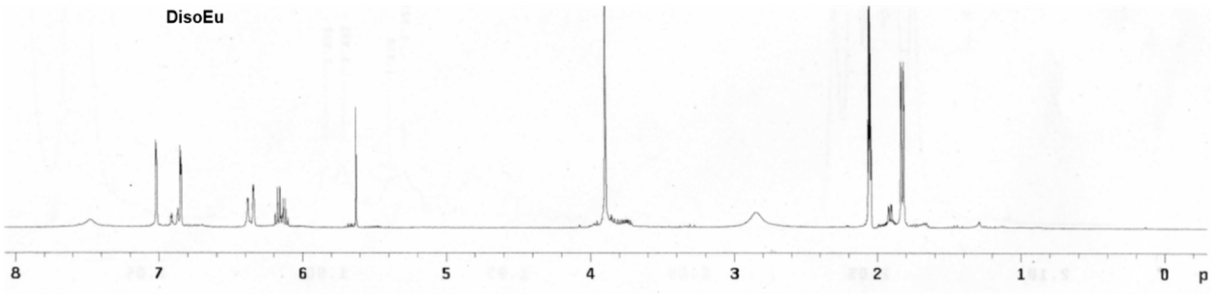
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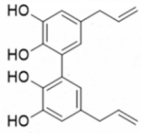
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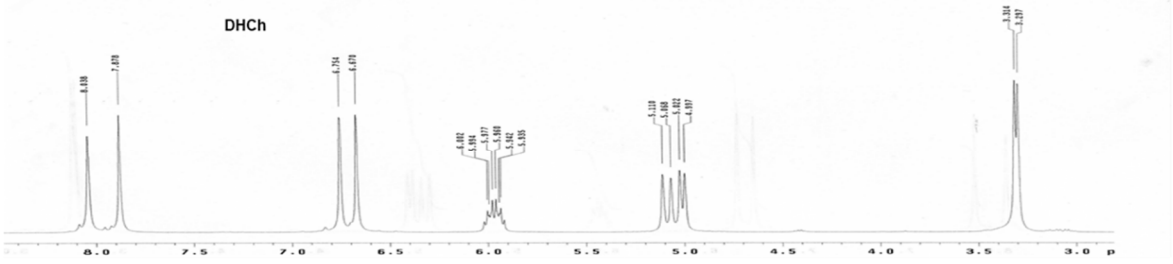
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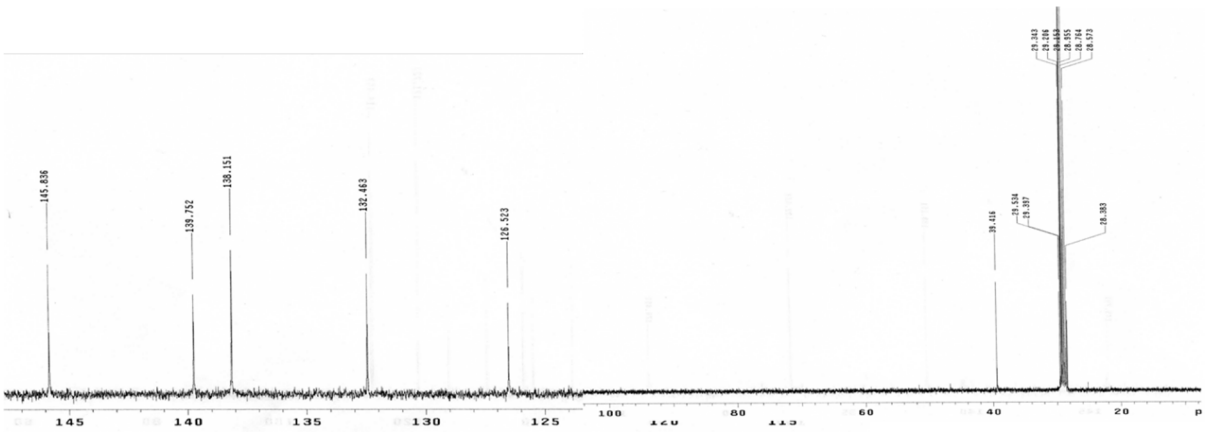
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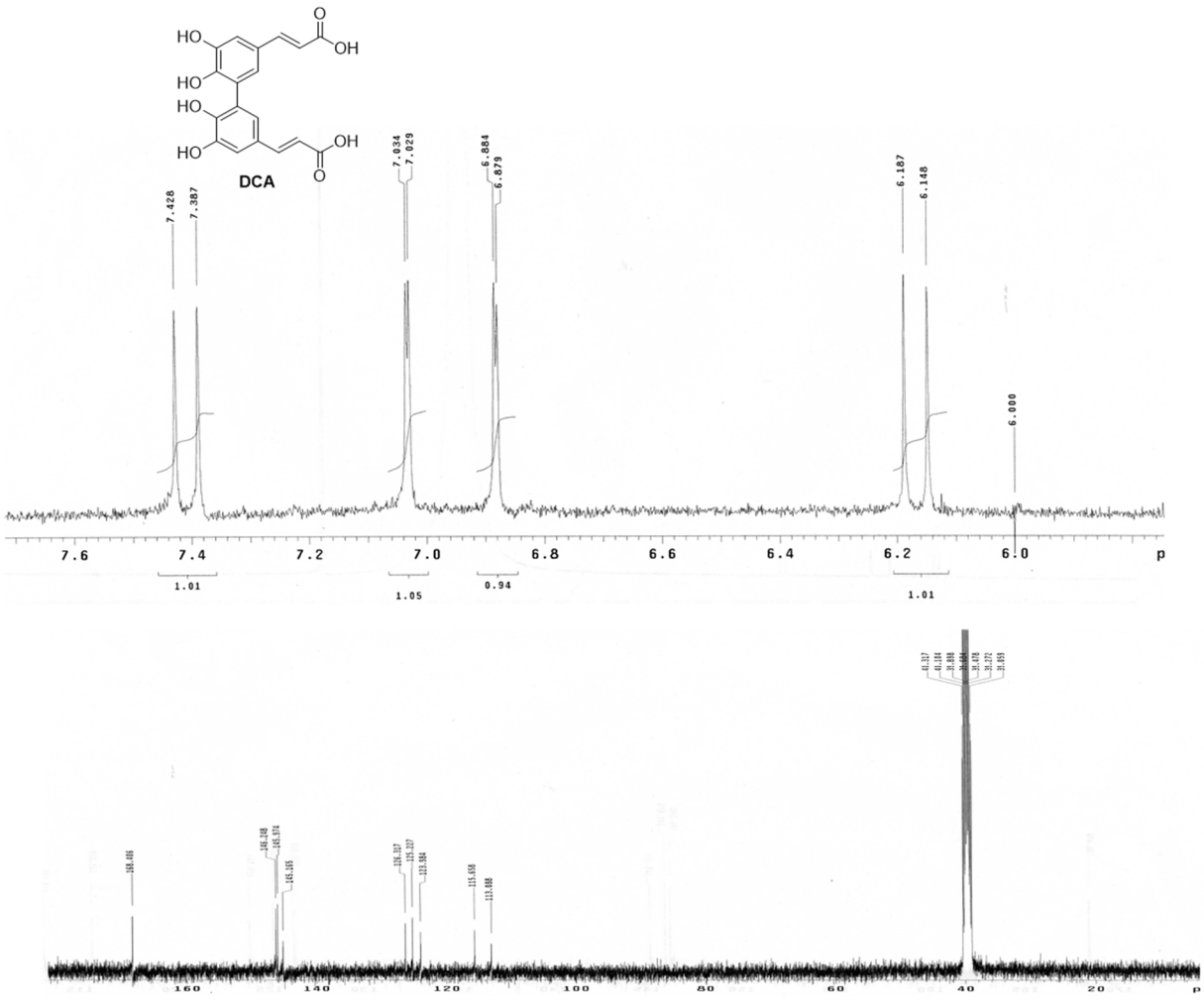
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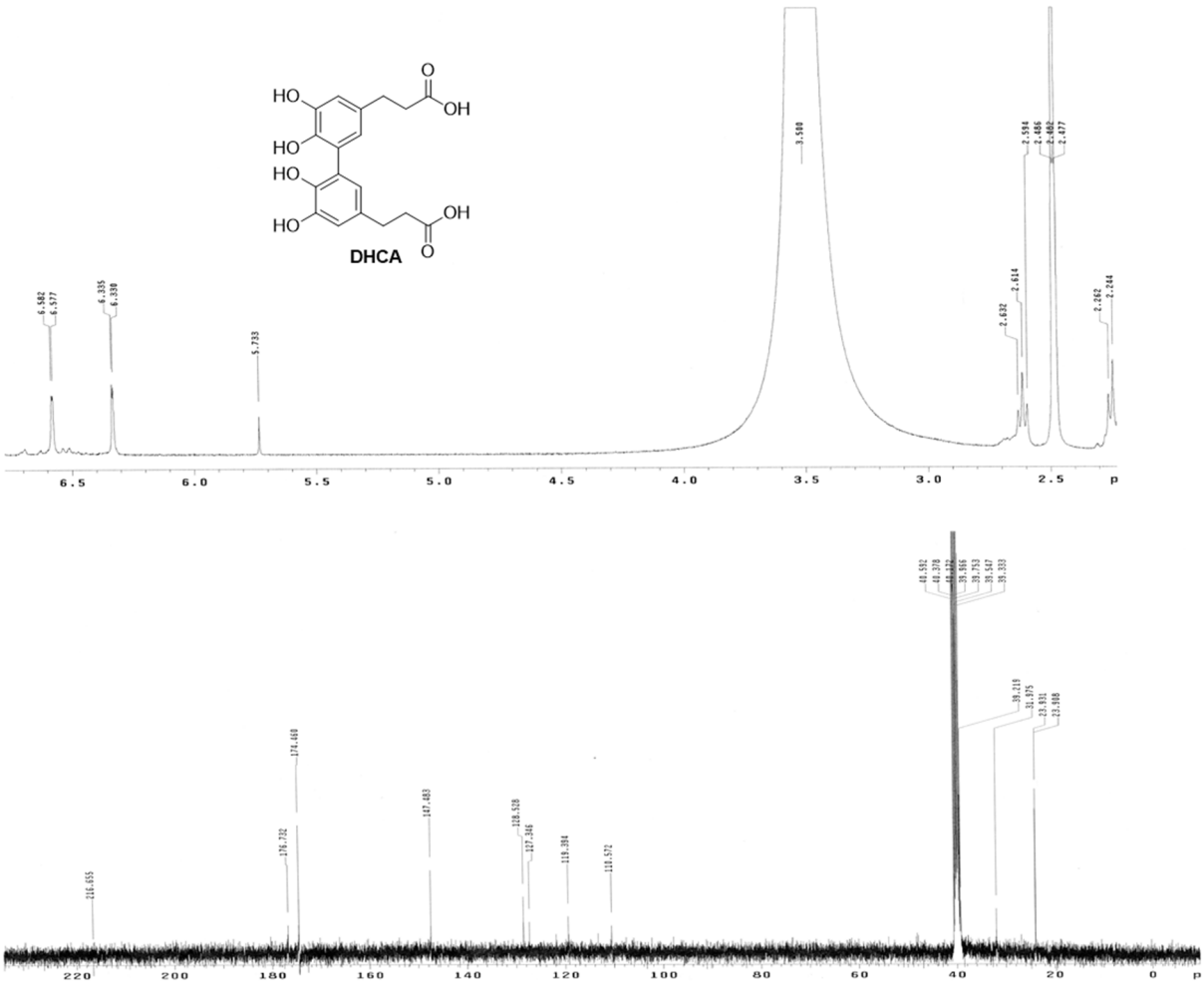

Figure S3. [1]H and 13C NMR spectra of **DisoEu**, **DHCh**, **DCA** and **DHCA**.

3. Lipid autoxidation

3.1. Lipid sample

Triacylglycerols of commercially available sunflower oil (TGSO) were cleaned from pro- and antioxidants by adsorption chromatography [3] and stored under nitrogen atmosphere at minus 20 °C. Fatty acid composition of the lipid substrate was determined according to Christie [4] by GC analysis of the methyl esters of the total fatty acids obtained with a GC-FID Hewlett-Packard 5890 equipment (Hewlett-Packard GmbH, Austria) and a capillary column HP INNOWAX (polyethylene glycol mobile phase, Agilent Technologies, USA) 30 m × 0.25 mm × 0.25 mm. The temperature gradient started from 165°C increased to 230 °C with 4°C/min and was held at this temperature for 15 min; injection volume was 1 μl. Injector and detector temperatures were 260 and 280 °C, respectively. Nitrogen was the carrier gas at a flow rate of 0.8 ml/min.

Lipid samples containing various inhibitors were prepared directly before use. Aliquots of the antioxidant solutions in acetone were added to the lipid sample. Solvents were removed under a nitrogen flow.

3.2. Lipid autoxidation

The process was carried out in a thermostatic bath at 80 °C (± 0.2 °C) by blowing air through the samples in special vessels and was monitored by withdrawing samples at measured time intervals and subjecting them to iodometric determination of the primary products (lipid hydroxyperoxides, LOOH) concentration, i.e. the peroxide value (PV) [5],[6]. All kinetic data are expressed as the average of two independent measurements.

TGSO is a mixture of different types of fatty acids glycerol esters, but only those fatty acids with pentadiene structures are vulnerable to oxidation by atmospheric oxygen. Phenolic antioxidants inhibit or retard lipid oxidation by interfering with either chain propagation or initiation by readily donating hydrogen atoms to lipid peroxyl radicals.

Scheme S1. Basic scheme of lipid (LH) autoxidation

Non-inhibited lipid (LH) autoxidation (in absence of an antioxidant)		
Chain generation	$2LH + O_2 \rightarrow \delta\ LO_2^{\bullet}$	(R_{IN})
Chain propagation	$LO_2^{\bullet} + LH\ (+O_2) \rightarrow LOOH + LO_2^{\bullet}$	(k_p)
Chain termination	$LO_2^{\bullet} + LO_2^{\bullet} \rightarrow P$	($2k_t$)
Chain branching 1	$LOOH\ (+O_2) \rightarrow \delta_1\ LO_2^{\bullet} + P_1$	(k_{b1})
Chain branching 2	$LOOH + LH\ (+O_2) \rightarrow \delta_2\ LO_2^{\bullet} + P_2$	(k_{b2})
Chain branching 3	$LOOH + LOOH\ (+O_2) \rightarrow \delta_3\ LO_2^{\bullet} + P_3$	(k_{b3})
Inhibiting reactions, responsible to the antioxidant activity of monomers M_iOH		
Chain termination with H atom transfer reaction (k_{Am})	$LO_2^{\bullet} + M_iOH \rightarrow LOOH + M_iO^{\bullet}$	
Chain termination with cross-recombination (k'_{Am})	$LO_2^{\bullet} + M_iO^{\bullet} \rightarrow$ inactive products	
Chain termination with homo-recombination (k_{tMO})	$2M_iO^{\bullet} \rightarrow$ inactive products	
Side reactions of $M_iO^{\bullet}$, decreasing the antioxidant activity of M_iOH		
Reverse inhibition reaction (k_{-Am})	$M_iO^{\bullet} + LOOH \rightarrow LO_2^{\bullet} + M_iOH$	
Additional propagation reaction (k_{pMO})	$M_iO^{\bullet} + LH\ (+O_2) \rightarrow \delta_3\ LO_2^{\bullet} + M_iOH$	
Quinoidal peroxides (QP) formation (k_{QP})	$2M_iO^{\bullet} + O_2 \rightarrow QP$	
Quinoidal peroxides (QP) decomposition	$QP\ (+ LH, + O_2) \rightarrow \delta_4\ LO_2^{\bullet} + P_4$	(k'_{QP})

In this mechanism: LH is linoleic acid with its allylic hydrogen; M_iOH - the studied monomeric *ortho*-metoxyphenol; $LO_2^{\bullet}$ - lipid peroxide radicals; $M_iO^{\bullet}$- phenoxyl radicals; P , P_A, P_1—P_4 – corresponding products formed; QP- quidoinal peroxides; R_{IN} - the rate of initiation; k_p, k_t, k_b, k_{Am}, k'_{Am} , k_{tMO}, k_{pMO}, k_{QP} – corresponding rate constants of different reactions.

In the presence of an antioxidant, the rate of hydroperoxides formation is related to the ratio of the lipid [LH] concentration to that of the antioxidant [M_iOH] concentration.

The classical rate laws for both uninhibited (R_c) and inhibited (R_A) lipid autoxidation, assuming the long chain approximation, are given by Eqs 1 and 2:

Rate of non-inhibited oxidation (R_c) $R_c=k_p [LH](R_{IN}/k_t)^{0.5}$ (1)

Rate of inhibited oxidation (R_{Am}) $R_{Am}=k_p[LH]R_{IN}/nk_{Am}[M_iOH]_0$ (2)

Inhibiting reactions, responsible to the antioxidant activity of the dimer $D_i(OH)_2$

Chain termination with H-atom transfer reaction:

$D_i(OH)_2+LO_2^{\bullet}\rightarrow D_i(OH)O^{\bullet}+LOOH$ (k_{Ad}) – the key reaction of inhibited lipid autoxidation

$D_i(OH)O^{\bullet}+LO_2^{\bullet}\rightarrow D_i(O^{\bullet})_2+LOOH$ (k'_{Ad}) [$D_i(O^{\bullet})_2$ –biradical of $D_i(OH)_2$; active intermediate]

Chain termination with cross recombination reaction:

$D_i(OH)O^{\bullet} + LO_2^{\bullet}\rightarrow D_i(OH)OL+O_2$ (active intermediate with one free OH group)

$D_i(O^{\bullet})_2 + 2LO_2^{\bullet}\rightarrow$ inactive products (k''_{Ad})

Chain termination with homo recombination reaction:

$2\ D_i(OH)O^{\bullet} \rightarrow [D_i(OH)O]_2$ - active intermediate with 2 free OH groups

Additional chain termination with H atom transfer reaction:

$D_i(OH)OL+LO_2^{\bullet} \rightarrow LOOH + D_i(O^{\bullet})OL$ - active intermediate

$[D_i(OH)O]_2 + 2LO_2^{\bullet}\rightarrow 2LOOH +$ inactive products

Additional cross-recombination reaction:

$D_i(O^{\bullet})OL +LO_2^{\bullet} \rightarrow$ inactive product

Additional homo-recombination reaction:

$2\ D_i(O^{\bullet})OL \rightarrow$ inactive product

Inhibited autoxidation - in presence of a biphenolic antioxidant $Q(OH)_2$

Termination (HAT) key reaction (k_{Aq})	$LO_2^{\bullet} + Q(OH)_2 \rightarrow LOOH + Q(OH)O^{\bullet}$	
Termination (Cross-dissproportionation)	$LO_2^{\bullet} + Q(OH)O^{\bullet} \rightarrow LOOH + Q(O)_2$	(k'_{Aq})
Termination (Homo-recombination)	$2Q(OH)O^{\bullet} \rightarrow$ Dimers	(k_{Rq})
Termination (Homo-dissproportionation) (k_{Dq})	$Q(OH)O^{\bullet} \rightarrow Q(OH)_2 + Q(O)_2$	

Scheme S2. Basic kinetic scheme of uninhibited and inhibited (in presence of monomers and dimers) lipid autoxidation.

Rate of inhibited oxidation (R_{Ad}): $R_{Ad}=k_p[LH]R_{IN}/nk_{Ad}[D_i(OH)_2]_0$ (3)

In Eqs 3-5: $k_p/(2k_t)^{0.5}$ is the oxidizability of the lipid substrate (linoleic acid glycerol ester); n- is the number of radicals trapped per inhibitor for molecule (the stoichiometric factor).

3.3.Determination of the main kinetic parameters of the studied compounds

Antioxidant efficiency means the potency of an antioxidant to increase the persistence towards oxidation of a lipid substrate by blocking the radical-chain

process. It was presented with a protection factor (PF) meaning how many times the antioxidant increases the persistence against oxidation of the lipid sample, determined as a ratio between the induction periods in presence (IP or IP_A) and in absence (IP_C) of an antioxidant, i.e. PF = IP_{Am}/IP_C for the monomers and PF = IP_{Ad}/IP_C for the dimers.

Inhibition degree (ID) is a measure of the antioxidant reactivity, which manifests how many times the antioxidant shortens the oxidation chain length, i.e. ID = R_C/R_{Am} in the case of monomers and ID = R_C/R_{Ad} in the case of dimers. For that reason, it is one of the most important kinetic parameters. Initial rates of lipid autoxidation in the absence (R_C) and in the presence of the antioxidant (R_{Am} or R_{Ad}) were found from the tangent at the initial phase of the kinetic curves of hydroperoxides accumulation.

Chain length of non-inhibited oxidation (ν_0)	$\nu_c = R_c/R_{IN}$
Chain length of inhibited oxidation (ν_{Am} or ν_{Ad})	$\nu_{Am} = R_{Am}/R_{IN}$ and $\nu_{Ad} = R_{Ad}/R_{IN}$
Inhibition degree (ID)	
In case of monomers	$ID = R_c/R_{Am} = \nu_c/\nu_{Am}$
In case of dimers	$ID = R_c/R_{Ad} = \nu_c/\nu_{Ad}$

4. Estimation of rate constant of antioxidant reaction with peroxyl radicals (k_A) using kinetic chemiluminescence (CL) method

$Y \rightarrow 2Y^{\bullet}$	(R_{IN})	
$Y^{\bullet} + O_2 \rightarrow YO_2^{\bullet}$		
$YO_2^{\bullet} + RH \rightarrow YOOH + R^{\bullet}$		
$R^{\bullet} + O_2 \rightarrow RO_2^{\bullet}$		
$RO_2^{\bullet} + RH \rightarrow ROOH + R^{\bullet}$	(k_p)	
$2RO_2^{\bullet} \rightarrow R{=}O^* + ROH + O_2$	($2k_t$)	
$RO_2^{\bullet} + M_iOH \rightarrow ROOH + M_iO^{\bullet}$	(k_{Am})	in case of monomers
$RO_2^{\bullet} + M_iO^{\bullet} \rightarrow$ *inactive products*	(k'_{Am})	
$RO_2^{\bullet} + D_i(OH)_2 \rightarrow ROOH + D_i(O^{\bullet})OH$	(k_{Ad})	in case of dimers
$RO_2^{\bullet} + D_i(O^{\bullet})OH \rightarrow ROOH + D_i(O^{\bullet})_2$	(k'_{Ad})	
$2RO_2^{\bullet} + D_i(O^{\bullet})_2 \rightarrow$ *inactive products*	(k''_{Ad})	

Scheme S3. Basic kinetic scheme of initiated oxidation of ethylbenzene (RH) in CL, in absence and in presence of studied compounds.

The CL assay for antioxidant activity is based on the competition between the self reaction of peroxy radicals (reaction step "k_t" in Scheme S2), giving rise to light emission, and scavenging the peroxy radicals by antioxidants (MOH), thus inhibiting the oxidation and thereby quenching the chemiluminescence [7]. The kinetic analysis of the reaction sequence (Scheme S3) affords convenient expressions relating the time profile of the chemiluminescence signal with the pertinent characteristics of an antioxidant being studied. The *strength* of an antioxidant is quantified by the rate constant k_A, whose value may be acquired from the slope of the chemiluminescence

time profile at the inflection point according to equation 4 [7] in which i_{rel} is a dimensionless light intensity given by the

$$(di_{rel}/dt)_{max} = 0.237(k_A/(2k_t)^{0.5})R_{IN} \quad (4)$$

ratio of the intensities in the presence (I) and in the absence (I_0) of an antioxidant, $i_{rel} = I/I_0$. It should be stressed that the consumption of an antioxidant in the chemiluminescence sample solution after the induction period results in recovery of the light-emission intensity, I_∞, i.e., $I_\infty = I_0$ and $i_{rel} = I/I_0 = I/I_\infty$, and R_{IN} stays for the reaction initiation rate defined by equation 5. In the latter expression, k_{dec} is the rate constant of the initiator (Y) decomposition

$$R_{IN} = 2\gamma_c k_{dec}[Y] \quad (5)$$

to generate initiating radicals (Y$^\bullet$ in Scheme S3) and γ_c is their probability to escape the solvent cage. The $2\gamma_c k_{dec}$ data are available for most of "standard" initiators (such as AIBN, for instance) in a number of organic solvents and in a temperature range of 20 to 80 °C. The $2\gamma_c k_{dec}$ data are available for most of "standard" initiators (such as AIBN, for instance) in a number of organic solvents and in a temperature range of 20 to 80 °C. Calculation of k_A from Eq. 4. was made taking into account that the $2k_t$ value obtained experimentally at the same conditions (chemiluminescence of ethylenbenzene) and temperature of 50 °C is equal to $2k_t = (1.90 \pm 0.05)\ 10^7\ M^{-1}s^{-1}$ [7].

Table S2. Effect of the 10-fold higher concentration of the studied antioxidants (0.1 mM and 1.0 mM). For monomers (M) PF^M_{10}=$PF_1/PF_{0.1}$ and ID^M_{10}=$PF_1/PF_{0.1}$, for dimers (D) $PF^D_{10} = PF_1/PF_{0.1}$ and $ID^D_{10} = ID_1/PF_{0.1}$

Monomer	PF^M_{10}	ID^M_{10}	PF^D_{10}	ID^D_{10}	Dimer
Cr	1.3	1.1	1.4	1.5	**DCr**
Va	1.2	1.0	n.s.	n.s.	**DVa**
Apo	1.2	1.3	n.s.	n.s.	**DApo**
Eu	1.3	1.2	n.s.	n.s.	**DEu**
iso-Eu	1.8	1.3	n.d.	n.d.	**DisoEu**
FA	1.6	2.8	1.8	2.3	**DFA**
HFA	1.6	2.8	1.7	2.9	**DHFA**
M1	3.5	6.3	5.2	13.9	**D1**
M2	3.2	5.5	3.6	5.5	**D2**
M3	3.0	3.2	4.4	3.5	**D3**
M4	2.0	4.0	3.0	5.0	**D4**
M5	3.0	2.2	3.0	3.7	**D5**
M6	n.d.	n.d.	n.d.	n.d.	**D6**
M7	n.d.	n.d.			
M8	2.9	4.7	4.1	3.0	**D8**
M9	2.2	3.4	4.1	5.4	**D9**

Curcumin	4.5	6.7	-	-	**-**

n.d. – not determined, n.s. not soluble in lipid substrate.

M6, M7, D6, D7, DisoEu were studied only by theoretical methods.

Table S3. Effect of biphenyl structure.

Dimer/Monomer		Conc. mM	$PF_{D/M}$	$ID_{D/M}$
D1/M1		0.1	2.6	2.9
		1.0	3.9	4.6
D2/M2		0.1	1.5	1.6
		1.0	1.7	1.6
D3/M3		0.1	1.5	1.0
		1.0	3.7	1.1
D4/M4		0.1	1.1	1.0
		1.0	1.7	1.2
D5/M5		0.1	1.0	2.4
		1.0	1.0	1.4
D8/M8		0.1	1.0	0.7
		1.0	1.3	0.7
D9/M9		0.1	1.0	0.7
		1.0	1.6	1.1
DFA/FA		0.1	1.0	1.0
		1.0	1.0	1.0
DCr/Cr		0.1	0.9	0.6
		1.0	2.0	1.0
Curc/M1		0.1	1.6	4.4
		1.0	3.9	4.7
Curc/M3		0.1	1.6	1.4
		1.0	2.4	3.0

5. DFT computational studies

Table S4. B3LYP/6-31+G(d,p) gas phase calculated enthalpies H_{298} (a.u.) and dihedral angles (°) for AO structures shown in Figure 1A-C and respective radicals (AO•). BDEs (kcal mol^{-1}) are derived from H_{298} values calculated for neutral (AO) and radical (AO•, H•) species.

Compound	**H_{298} (AO)**	**H_{298} (AO•)**	**BDE**	**θ ° (AO)**	**θ ° (AO•)**	Also mentioned in:
Curcumin	-1263.272328	-1262.646509	78.8			[8]

Cr	-461.169138	-460.541707	79.8			[9]
Va	-535.200734	-534.567085	83.7			[9]
Apo	-574.496592	-573.863718	83.2			[9]
Eu	-538.531135	-537.903146	80.1			[9]
isoEu	-538.541134	-537.917493	77.4			[9]
FA	-687.821912	-687.193184	80.6			[10]
M1	-1302.554493	-1301.928076	79.2			[10]
M3	-1032.317391	-1031.689946	79.8			
M6	-804.486573	-803.859376	79.6			
M7	-843.773289	-843.146109	79.9			
M2	-653.066142	-652.438022	80.2			[10]
HFA	-689.020063	-688.391341	80.6			
M4	-805.682054	-805.054012	80.2			
M5	-997.374041	-996.745838	80.3			
M8	-1036.666595	-1036.038505	80.2			[11]
M9	-1154.525497	-1153.897424	80.2			[11]
HCh	-499.257728	-498.641117	73.0			
HPh	-612.594197	-611.975469	74.3			
CA	-648.548130	-647.928078	75.2			[12]
HCA	-649.745959	-649.129776	72.7			
DCr	-921.154915	-920.528642	79.1	62.9	61.1	[9]
DVa	-1069.218727	-1068.586389	82.9	62.7	59.5	[9]
DApo	-1147.810582	-1147.178797	82.5	63.0	60.4	[9]
DEu	-1075.878884	-1075.252057	79.4	63.0	61.1	[9]
DisoEu	-1075.899195	-1075.276325	76.9	63.5	62.9	[9]
DFa	-1374.461072	-1373.833542	79.9	63.1	60.3	[10],[12]
D1	-1302.554462	-1301.928383	78.9	63.6	60.5	[10],[12]
D3	-2063.452014	-2062.825554	79.2	63.0	61.7	
D6	-1607.790268	-1607.164203	78.9	63.0	60.6	
D7	-1686.363704	-1685.737657	78.9	62.8	60.6	
D2	-1304.948860	-1304.321729	79.6	62.2	59.7	[10]
DHFA	-1376.853281	-1376.225057	80.3	63.6	60.6	
D4	-1610.180433	-1609.553451	79.5	63.9	60.5	
D5	-1993.565020	-1992.938034	79.5	63.1	61.9	
D8	-2072.150177	-2071.523306	79.4	62.3	60.9	[11]
D9	-2307.867988	-2307.867988	79.6	63.2	61.5	[11]
DHCh	-997.331996	-996.716674	72.2	62.8	61.3	
DHPh	-1224.005687	-1223.387443	74.0	63.2	62.0	
DCA	-1295.913311	-1295.293777	74.8	62.5	60.8	
DHCA	-1298.307686	-1297.691985	72.4	62.6	61.1	

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