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Antioxidant activity of selected *o*-methoxyphenols and biphenols: theoretical and experimental studies

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A combination of theoretical and experimental approaches was applied to study and to explain the structure – antioxidant activity relationship for selected *ortho*-methoxyphenols (natural and natural-like phenols). The corresponding dimers (biphenols) possessing guaiacyl moiety were handpicked in order to study the influence of the conformation and substituents in the aromatic ring on the antioxidant activity. Chain-breaking antioxidant activities of the compounds under study were determined from the kinetic curves of bulk lipid autoxidation. Full geometry optimization of neutral molecules and their corresponding phenoxyl radicals for all compounds under study were obtained by using DFT (B3LYP/6-31+G**) calculations. Good correlation between experimental and predicted activity was achieved which is helpful for the structure-activity relationship explanation.

Keywords: Antioxidants, Protective effect, Bulk lipid autoxidation, Natural phenols, Hydroxylated biphenyls, DFT calculations

INTRODUCTION

Antioxidants act as chain-breaking agents by transferring a hydrogen atom to peroxyl radicals at a rate higher than the propagation reaction, as a result, conversion of peroxyl radicals into non-radical products occurs [1,2]. Currently there is a great interest in friendly antioxidants as a replacement for the toxic ones (such as butylated hydroxytoluene, BHT) commonly used in foods, cosmetics and fragrances [3]. The reactions of peroxyl radicals with the phenol OH group of an effective phenolic antioxidant are much faster than those with C-H bond [4]. Naturally occurring phenols are a valuable source of bioantioxidants [5, 6] which are associated with a vast array of useful biological activities, especially antimicrobial and anti-inflammatory properties [7, 8]. Nowadays, there is a strong interest in drugs and food additives. Food supplements in combination with drugs having two or more actions (e.g. antioxidant and anti-inflammatory), targeted at multiple etiologies of the same disease, may offer a great therapeutic benefit.

2-Methoxy phenol is one of the common classes of secondary metabolites in medicinal plants [9, 10]. When these phenols, characterized by a guaiacyl unit, are substituted at position 4 with an electron donating group (EDG), the guaiacyl unit makes the compound a potential antioxidant. This is due to the favoured stabilization of the generated phenoxyl radical by forming a five-membered ring with the methoxyl group and the EDG group in *para* position to the phenol OH group [11]. The antioxidant properties of several natural phenols, like eugenol (**Eu**), creosol (**Cr**), apocynin (**Apo**) and isoeugenol (***iso*Eu**), have already been reported [12-14] and the protective effect in different oxidant systems and biosystems has been assessed [15, 16]. They are constituents of spices, flavours and fragrances. Eugenol (**Eu**) efficiently inhibits the metal-mediated low density lipoprotein (LDL) oxidation acting as a physiological antioxidant *in vivo* [15] and apocynin (**Apo**) is an efficient inhibitor of the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase complex [16].

Hydroxylated biphenyls are widely present in nature and conversely to their corresponding natural monomeric phenols, they represent an important source of bioactive compounds that has not been well investigated [17]. Structurally they are dimers of phenols where two aromatic rings are C-C single bond bridged. The presence of hydroxylated functionalities in the biphenyl structure provides interesting features in terms of bioavailability, interactions with proteins and antioxidant activities [18, 19]. Compared to phenols, often, hydroxylated biphenyls are less toxic than the corresponding phenolic monomer [20] from which they are produced by oxidative coupling reaction. Some of the hydroxylated biphenyls have been already isolated from many plants and characterized [21], others are still undiscovered. Dehydrodieugenol (**DEu**) has been isolated from the buds of clove (*Syzygium*

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aromaticum) and, structurally, it represents a C_2-symmetrical dimer of **Eu** [22]. **DEu** manifests interesting antimutagenic activity, compared to its monomer it is less toxic and possesses higher antioxidant activity on lipid peroxidation [23]. Similarly, the dimer of apocynin (**DApo**), detected in biological systems treated with apocynin (**Apo**), manifests higher anti-inflammatory and antioxidant activities in comparison to its corresponding monomer **Apo** [24]. Considering the increased lipophilicity of the dimers compared to monomers and the role they can play in delaying the cellular damage due to membrane lipid peroxidation, an investigation of natural phenols (monomers and dimers) on bulk lipid oxidation appears useful and strategic for further studies on the effect of natural bioactive phenols in biological systems.

The aim of this work was to prepare a small collection of hydroxylated biphenyls starting from the corresponding natural phenol monomers, commercially available, and to study their effect during bulk lipid autoxidation in comparison with their corresponding monomers (Figure 1). We selected 2-methoxy phenol monomers as creosol (**Cr**), vanillin (**Va**), apocynin (**Apo**), eugenol (**Eu**) and their corresponding dimers **DCr**, **DVa**, **DApo**, **DEu**, respectively (Figures 1a and 1b). Antioxidant activity of the monomers was also compared with that of isoeugenol (***iso*Eu**), a 2-methoxy phenol known for the high antioxidant activity [15]. The structure-activity relationship was investigated by Density Functional Theory (DFT) calculation of monomers and dimers with the aim to identify structural parameters able to decrease the bond dissociation enthalpy (BDE) of the phenol OH bond and to stabilize the phenoxyl radical.

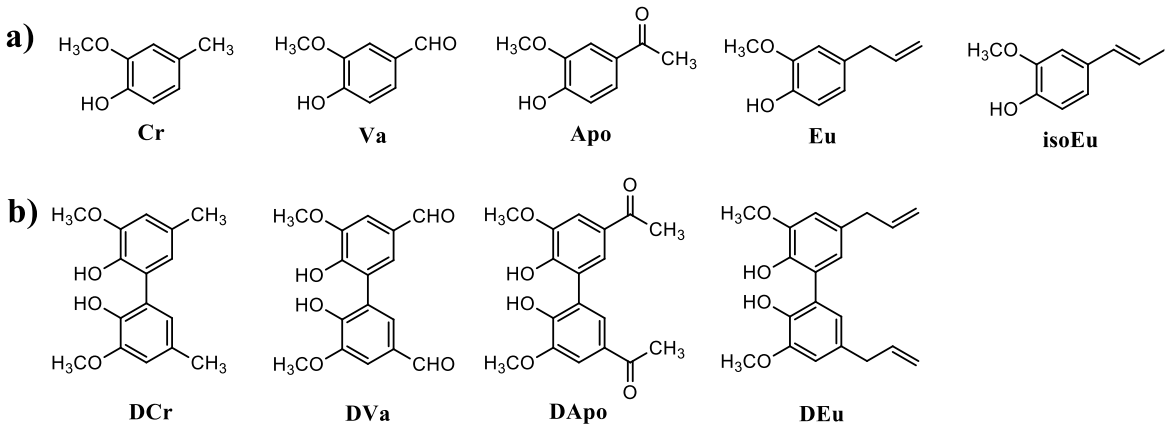


Figure 1. Structures of the studied compounds: a) 2-methoxy phenol monomers; b) hydroxylated biphenyls.

EXPERIMENTAL AND COMPUTATIONAL DETAILS

Experimental details

All ^{1}H NMR and ^{13}C NMR spectra were recorded on a spectrometer Varian Mercury Plus operating at 399.93 MHz and 100.57 MHz, respectively. Chemical shifts are given in ppm (δ) and coupling constants in Hertz. $CDCl_3$, acetone-d_6, were used as solvents as indicated below. Shifts are given in ppm relative to the remaining protons of the deuterated solvents used as internal standards (^{1}H, ^{13}C). All reagents were of commercial quality and used as purchased from various producers (Sigma-Aldrich, Merck). Flash chromatography was carried out with silica gel 60 (230-400 mesh, Kiesgel, EM Reagents) eluting with an appropriate solution in the stated v:v proportions. Analytical thin-layer chromatography (TLC) was performed with 0.25 mm thick silica gel plates (Polygram® Sil G/UV$_{254}$, Macherey-Nagel). The purity of all new compounds was judged to be >98% by ^{1}H-NMR spectral determination. Biphenyls **DEu**, **DVa** and **DApo** were prepared as previously described by us [25-27]. Solvents were used without additional purification or drying, unless otherwise noted.

2,2-Dihydroxy-3,3-dimethoxy-5,5-dimethyl-1,1-biphenyl (dehydrodicreosol, **DCr***)*

To a solution of 2-methoxy-4-methylphenol (creosol **Cr**) (0.5 g, 3.6 mmol) in dry dichloromethane (25 mL), was added dropwise a solution of methyl-*t*-butyl ammonium permanganate (MTBAP) (0.57 g, 1.8 mmol) in dry dichloromethane (15 mL) under nitrogen at 0°C. The solution was stirred for 30 min at 0 °C. Aqueous $Na_2S_2O_5$ was added to the mixture, the organic layer was dried over Na_2SO_4 and removed under reduced pressure to obtain a brown solid. The product obtained was washed twice with pentane (2×50 mL) to yield 0.42 g (85%) of the dimer **DCr** as a light yellow solid. Mp 133-135 °C (Lit. [28] 132-134 °C); ^{1}H NMR ($CDCl_3$) δ 2.34 (s, 6H, CH_3), 3.91 (s, 6H, OCH_3), 6.0 (bs, 2H, OH), 6.72-6.74 (m, 4H, ArH); ^{13}C NMR ($CDCl_3$) δ 21.10, 56.06, 111.31, 123.43, 124.40, 129.64, 140.33, 147.09;

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61; Found: C, 70.10; H, 6.66.

Biphenyls **DEu**, **DCr**, **DVa**, and **DApo** were prepared starting from the corresponding monomers **Eu**, **Cr**, **Va**, and **Apo**, respectively, following known coupling reaction procedures with slight modifications carried out by us to improve yields and make the methodology more straightforward. Although all monomers belong to the family of 2-methoxy phenols, substitution at *para* position to phenol-OH group required different oxidative conditions and reagents. **Eu** was treated with a solution of NH_4OH and $K_3Fe(CN)_6$ in acetone-water at room temperature in open air. **DEu** was obtained as a colorless solid in 95% yield after recrystallization from absolute ethanol [25]. Regioselective dimerization of **Va** in the presence of the oxidant mixture $K_2S_2O_8/FeSO_4$ in water-acetone at 50 °C, gave **DVa** by precipitation. The solid, after dissolution in aqueous NaOH and further acidification, was collected in 95% yield [26]. **Apo** was treated with a stoichiometric amount of $K_2S_2O_8/FeSO_4$ at room temperature in open air using a mixture of water/acetone as solvent. **DApo** was obtained in 80% yield without further purification [27]. **DCr** was obtained in good yield following a known procedure by reaction of **Cr** with methyl-*t*-butyl ammonium permanganate in dichloromethane at room temperature [28].

Chain-breaking antioxidant activity: Triacylglycerols of commercially available sunflower oil (TGSO) were cleaned from pro- and antioxidants by adsorption chromatography and stored under nitrogen at temperature 20 °C. Fatty acid composition of the lipid substrate was determined by GC analysis of the methyl esters: 16:0 (6.7%); 18:0 (3.6%); 18:1 (25.1%); 18:2 (63.7%); 20:0 (0.2%); 22:0 (0.7%); the numbers x:y indicate the number of carbon atoms and double bonds in the fatty acid, respectively. Lipid samples containing various inhibitors were prepared directly before use. Aliquots of the antioxidant solutions in purified acetone were added to the lipid sample. Solvents were removed under a nitrogen flow.

Lipid autoxidation: The process was carried out in a thermostatic bath at 80±0.2 °C by blowing air through the samples in special vessels. The oxidation process 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). All compounds were subjected to lipid autoxidation at 80 °C at two concentrations, 0.1 and 1.0 mM, respectively. All kinetic data are expressed as the average of two independent measurements which were processed using the computer programmes Origin 6.1 and Microsoft Excel 2010. The basic kinetic scheme of lipid autoxidation is published elsewhere [29].

Determination of the main kinetic parameters of the studied compounds [30-32]:

Protection factor (PF) is a measure for the antioxidant efficiency i.e. $PF = IP_A/IP_C$ and means how many times the oxidation stability of a lipid substrate increased in presence of an antioxidant. IP_C and IP_A are the induction periods of control sample and in presence of an inhibitor.

Inhibition degree (ID) is a measure of the antioxidant reactivity, e.g. how many times the antioxidant shortens the oxidation chain length, i.e. $ID = R_C/R_A$. The initial oxidation rates R_C in the absence and R_A in the presence of antioxidant were found from the tangent at the initial phase of the kinetic curves of hydroperoxides accumulation.

Antioxidant capacity (Rm) is a measure of the consumption of the antioxidant during the induction period.

Radical scavenging activity: the capacity of studied compounds to scavenge free radicals was estimated by the DPPH radical test in acetone solution. Experimental details are previously presented [33]. The main kinetic parameters of the process are radical scavenging activity (%RSA), rate constants of radical reactions between DPPH radical and studied compounds (k_{RSA}) and stoichiometric coefficient (n) that shows how many radicals are trapped by one molecule of antioxidant. All these kinetic parameters were determined and compared.

Computational details

Unrestricted open-shell approach UB3LYP [34] and 6-31+G(d,p) [35, 36] basis set were used to optimize the geometry of compounds studied and their radicals without symmetry constraints with the default convergence criteria using the Gaussian 09 program [37]. Frequency calculations for each optimized structure were performed at the same level of theory. No imaginary frequency was found for the lowest energy configurations of any of the optimized structures. Unscaled thermal corrections to enthalpy were added to the total energy values. The BDEs for the generation of the respective radicals from the parent compounds were calculated by the formula:

$$BDE = H_{298}(AO^{\bullet}) + E_T(H^{\bullet}) - H_{298}(AOH) \quad (1)$$

where $H_{298}(AO^{\bullet})$ and $H_{298}(AOH)$ are enthalpies calculated at 298 K for radical species, $AO^{\bullet}$ and

neutral molecule AOH, respectively, $E_T(H^\bullet)$ (calculated total energy of $H^\bullet$) is -313.93 kcal mol^{-1}. Solvation effects were accounted for by employing the polarizable continuum model (PCM) [38] as implemented in the Gaussian 09 suite of programs: all structures were optimized in acetone and DMSO surrounding environments. PyMOL molecular graphics system was used for generation of the molecular graphics images [39].

RESULTS AND DISCUSSION

Chain breaking antioxidant activity

The effect of monomers' concentration during bulk lipid autoxidation was studied at 0.1 and 1.0 mM, respectively, as depicted in Figures 2 and 3.

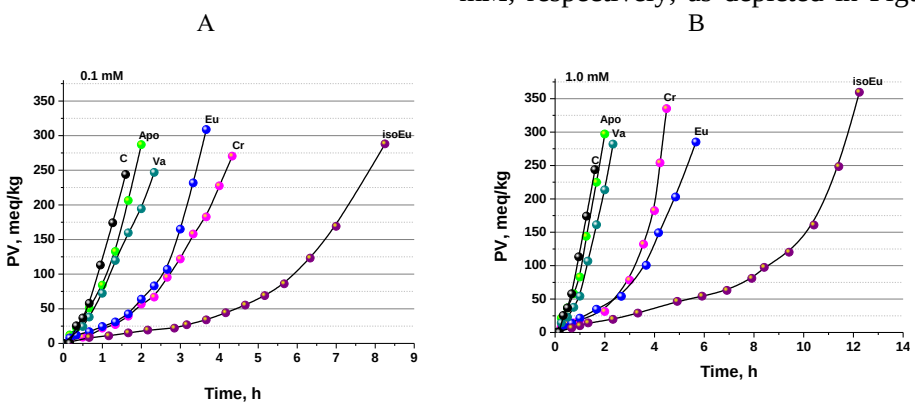


Figure 2. Kinetics of TGSO autoxidation at 80° C in absence (control sample, C) and in presence of A) 0.1 mM and B) 1.0 mM of the studied monomers.

The main kinetic parameters (PF, ID, Rm) are reported for all studied monomers (Table 1) evidencing the highest chain-breaking antioxidant efficiency and reactivity of ***iso*Eu** at both concentrations. New orders of antioxidant efficiency (PF), reactivity (ID) and capacity (Rm) were obtained for both studied concentrations:

Low concentration (0.1 mM)

PF: isoEu (5.7) > Cr (2.7) ≥ Eu (2.5) > Va (1.1) = Apo (1.1)

ID: isoEu (5.2) > Cr (3.3) > Eu (2.4) > Va (1.3) > Apo (0.9)

Rm 10^{-8}: isoEu (0.5) < Cr (1.0) < Eu (1.1) < Va (2.5) = Apo (2.5)

High concentration (1.0 mM)

PF: isoEu (10.1) > Cr (3.6) > Eu (3.2) > Va (1.3) = Apo (1.3)

ID: isoEu (6.9) > Cr (3.5) > Eu (2.9) > Va (1.3) > Apo (0.7)

Rm 10^{-8}, M/s: isoEu (2.7) < Cr (7.7) < Eu (8.7) < Va (21.4) = Apo (21.4)

From the main kinetic parameters the antioxidant activity of the studied compounds was evaluated. The highest antioxidant activity was observed for ***iso*Eu**. Moderate activities for **Cr** and **Eu** were deduced. **Va** and **Apo** have no activity in our model system of lipid autoxidation and this can be explained with their structures. The presence of electron-withdrawing group (EWD) in the latter two monomers hampers the formation of radical species and their stabilization. Moreover, their participation in side reactions with LOOH should not be ruled out.

*Iso*Eugenol is the most effective antioxidant. This can be explained with the presence of a vinyl double bond in the side chain favoring an extended conjugation with the aromatic ring when a radical methide is generated. **Cr** and **Eu** are effective chain-breaking antioxidants as a result of their participation in "homo-disproportionation" reactions (Schemes 1 and 2) allowing regeneration of the antioxidant.

Both **DVa** and **DApo** dimers are completely insoluble in acetone (our reference solvent for the monomers) and in triglycerides, so they could not be tested in our system. Due to the partial solubility of **DEu** in acetone, it was dissolved at the minimum concentration of DMSO (49 mM) and then assayed in bulk lipid autoxidation as shown in Figure 4. **DCr** is soluble in acetone, but its activity in the same acetone/DMSO mixture was tested in order to be compared with that of **DEu.** It was shown that in presence of DMSO the capacity of both studied dimers to inhibit bulk lipid autoxidation decreases. The effect is more pronounces for the dimeric structures in comparison to the monomeric ones.

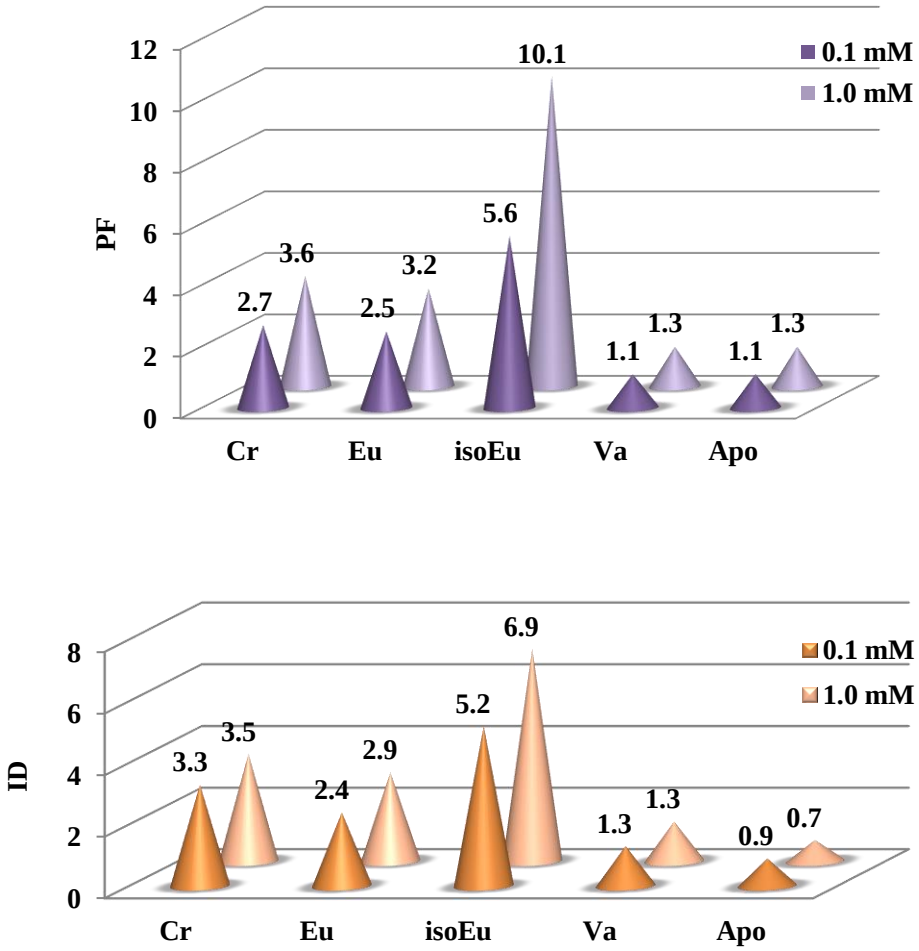
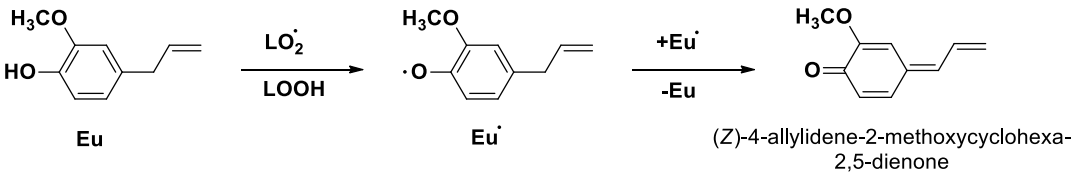


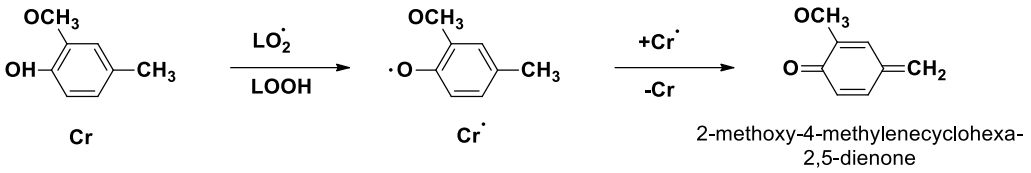
Figure 3. Protection factor (**PF**) and inhibition degree (**ID**) of studied monomers for both concentrations (0.1 mM and 1.0 mM).

Table 1. Main kinetic parameters, characterizing TGSO autoxidation at 80˚C in presence of 0.1 mM and 1.0 mM of the test compound. For control sample: IP_C = (1.0 ± 0.2) h, $R_C = 8.3\times10^{-6}$ M /s.

Compd	Concentration	IP_A, h	PF -	R_A 10^{-6}, M/s	ID -	Rm 10^{-8}, M/s	RRm 10^{-3}, -	Activity
Cr	0.1	2.7±0.2	2.7	2.5±0.2	3.3	1.0±0.2	4.0	Moderate
	1.0	3.6±0.3	3.6	2.4±0.2	3.5	7.7±0.4	32.1	moderate
Eu	0.1	2.5 ±0.2	2.5	3.4±0,3	2.4	1.1±0.2	3.2	moderate
	1.0	3.2±0.3	3.2	2.9±0.3	2.9	8.7±0.4	30.0	moderate
isoEu	0.1	5.6±0.5	5.6	1.6±0.3	5.2	0.5±0.03	3.1	strong
	1.0	10.1±0.8	10.1	1.2±0.2	6.9	2.7±0.2	22.5	strong
Va	0.1	1.1±0.2	1.1	6.4±0.5	1.3	2.5±0.2	3.9	no activity
	1.0	1.3±0.2	1.3	6.5±0.5	1.3	21.4±2.0	32.9	no activity
Apo	0.1	1.1±0.1	1.1	9.1±0.5	0.9	2.5±0.2	2.8	no activity
	1.0	1.3 ±0.2	1.3	11.6±0.9	0.7	21.4±2.0	18.4	no activity



Scheme 1. Reaction mechanism of eugenol.



Scheme 2. Reaction mechanism of creosol.

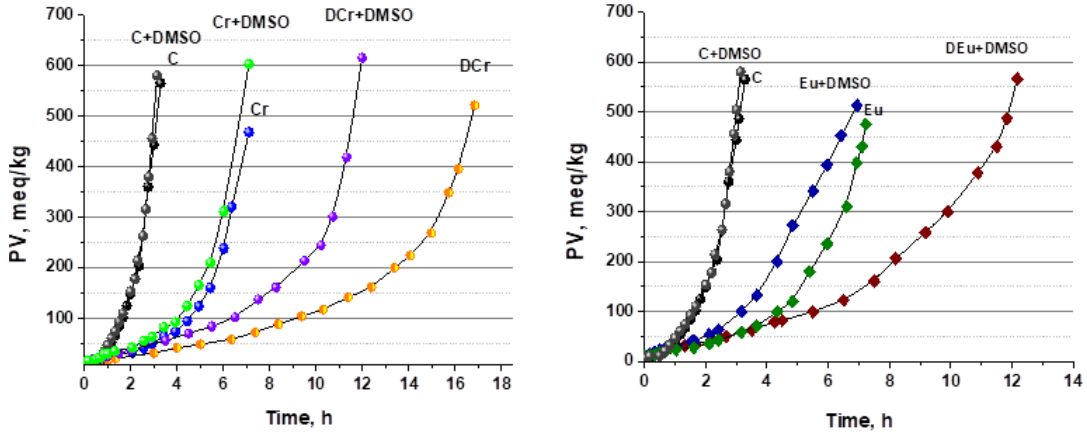


Figure 4. Kinetic curves of lipid hydroperoxides accumulation during TGSO autoxidation at 80 °C in absence (control sample, C) and in presence of 1.0 mM of studied couples: **Cr**/**DCr**, **Eu**/**DEu**, in absence and in presence of 49 mM DMSO.

Table 2. Main kinetic parameters in the presence of 1.0 mM of **Cr**, **Eu** and their corresponding dimers in 49 mM DMSO (effect of solvent) under TGSO autoxidation at 80° C. For control sample: IP_C=2.0 h, R_C=3.4 10^{-6} M/s, IP_{C+DMSO}=2.0 h, R_{C+DMSO}=2.9 10^{-6} M/s.

Compounds	IP_A, h	PF-	R_A 10^{-6}, M/s	ID -	Rm 10^{-8}, M/s	RRm 10^{-3}, -	Activity
Cr	5.2±0.5	2.6	1.5±0.2	2.27	5.37±0.3	35.87	moderate
Cr + DMSO	5.1±0.5	2.6	2.7±0.1	1.07	5.42±0.3	20.07	moderate
DCr	14.3±0.8	7.2	1.1±0.1	3.21	1.94±0.2	18.3	strong
DCr + DMSO	10.3±0.6	5.2	1.4±0.2	2.09	2.70±0.2	19.4	strong
Eu	5.5±0.5	2.8	1.9±0.2	1.83	5.05±0.3	27.15	moderate
Eu + DMSO	3.3±0.2	1.7	3.4±0.5	0.86	8.42±0.4	24.9	moderate
DEu + DMSO	10.2±0.6	5.1	2.8±0.5	1.04	2.71±0.2	9.7	strong

The results presented in Table 3 show higher radical scavenging activity towards DPPH radical for all dimers than that for the corresponding monomers of the studied compounds. This finding is in agreement with the chain-breaking antioxidant activity during bulk lipid autoxidation.

DFT calculations

The geometries of all parent compounds and possible phenoxyl radical species were optimized at UB3LYP/6-31+G(d,p) level. The optimized geometries only of the thermodynamically preferred rotamers of the parent compounds are presented in Figure 5. Complete geometrical parameters of all investigated systems are available on request. Theoretically calculated parameters characterizing the parent compounds (monomers and dimers) and the radical species (radicals and biradicals) are collected in Table 4. The BDEs derived from the respective enthalpy values are also presented graphically in Figure 5. The BDE values in gas phase, acetone and DMSO are compared.

Table 3. Main kinetic parameters of radical scavenging activity for studied compounds.

Compound	Time, min	Concentration, μM					
		25			39		
		RSA, %	n	k_{RSA} $M^{-1}s^{-1}$	RSA, %	n	k_{RSA} $M^{-1}s^{-1}$
Eu	<1 min			1.2			1.6
	2 min	0.37	0.01		0.74	0.02	
	20 min	2.03	0.08		3.58	0.09	
DEu	<1 min			49.6			49.7
	2 min	10.35	0.40		16.2	0.39	
	20 min	28.36	1.08		41.7	0.98	
Cr	<1 min			4.4			3.3
	2 min	1.10	0.05		1.31	0.03	
	20 min	4.01	0.16		5.28	0.14	
DCr	<1 min			19.1			31.8
	2 min	4.94	0.20		12.4	0.31	
	20 min	17.33	0.68		39.5	0.97	
Apo	<1 min			0.6			1.0
	2 min	0.26	0.01		0.52	0.01	
	20 min	0.63	0.03		1.18	0.03	
DApo	<1 min			3.4			3.4
	2 min	0.87	0.04		1.38	0.04	
	20 min	2.06	0.08		2.93	0.08	

BDE calculations confirmed the results obtained during bulk lipid autoxidation of monomers. For the series of the monomeric species the BDE values range between 77.41 and 83.69 kcal/mol in the gas phase, 73.28 and 81.47 kcal/mol in acetone medium, 73.70 and 81.71 kcal/mol in DMSO. **IsoEu** is characterized with the lowest BDE values both in the gas phase and in solvents confirming the best antioxidant activity. The high **Apo** (r) and **Va** (r) BDEs evidence the inability of the compounds to generate and stabilize a radical. A similar BDEs trend was estimated for radical **DApo** (r) and **DVa** (r), both unable to generate stable radicals. All C-C bridged dimers were characterized with lower BDE for radical species generation than the respective monomers, the lowest values were calculated for **DEu** and **DCr** (79.36 and 79.05 kcal/mol in the gas phase, respectively). The BDEs calculated for the biradical species (**br**) generation are higher than those for the first H-atom abstraction. It is known that in an *ortho-ortho* biphenol structure the pKa of the second phenol OH group is higher compared to the first one, thus, it is reasonable to expect a similar behavior also in the biradicals species formation (higher BDE values). C_2-symmetric dimer originating from ***iso*Eu** dimer was not considered because it does not exist in nature [40]. The spin density values at the oxygen atom (**O•**) from the hydroxyl group (listed also in Table 4) are not characteristic for the antioxidant activity.

A conclusion can be drawn (from the theoretical calculations) that **Eu**, **IsoEu**, **Cr** and their dimers are expected to be better antioxidants than **Apo** and **Va**. All dimeric structures have lower BDEs in comparison to the respective monomeric species.

CONCLUSIONS

A set of natural phenols known for their valuable biological activity was assayed in bulk lipid autoxidation and their chain-breaking antioxidant efficiency and reactivity were compared with those for the corresponding C_2-symmetric dimers soluble in acetone or DMSO. The dimers showed stronger antioxidant effectiveness, in particular **DCr** (that possesses a methyl group in *para* position to the guaiacyl unit). BDEs were calculated for all compounds and a good correlation with the experimental data was found. The results presented herein can motivate a deeper study of C_2-symmetric dimers of natural phenols in a combinatory drug therapy where the antioxidant activity plays an important role.

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Table 4. UB3LYP/6-31+G(d,p) calculated enthalpies (H_{298}) at 298 K (Hartree) in the gas phase, BDE (kcal/mol) and spin density (e^-).

Compound	H_{298}	BDE			Spin density at O$^\bullet$
		gas phase	acetone	DMSO	
		Monomers			
Apo	-574.496591				
Apo (r)	-573.863719	83.21	80.64	80.92	0.33
Eu	-538.531134				
Eu (r)	-537.903146	80.14	76.41	76.79	0.36
IsoEu	-538.541134				
IsoEu (r)	-537.917493	77.41	73.28	73.70	0.31
Cr	-461.169137				
Cr (r)	-460.541662	79.82	75.86	76.27	0.36
Va	-535.200736				
Va (r)	-534.567087	83.69	81.47	81.71	0.32
		Dimers			
DApo	-1147.810582				
DApo (r)	-1147.178797	82.53	80.20	80.49	0.31
DApo (br)	-1146.545817	83.27	80.61	80.95	0.31
DEu	-1075.878887				
DEu (r)	-1075.252146	79.36	75.93	76.26	0.34
DEu (br)	-1074.624177	80.13	76.29	76.71	0.34
DCr	-921.154892				
DCr (r)	-920.528641	79.05	75.40	75.81	0.35
DCr (br)	-919.901109	79.86	75.81	76.27	0.35
DVa	-1069.218675				
DVa (r)	-1068.586389	82.84	80.88	81.13	0.30
DVa (br)	-1067.952627	83.77	81.37	81.69	0.30

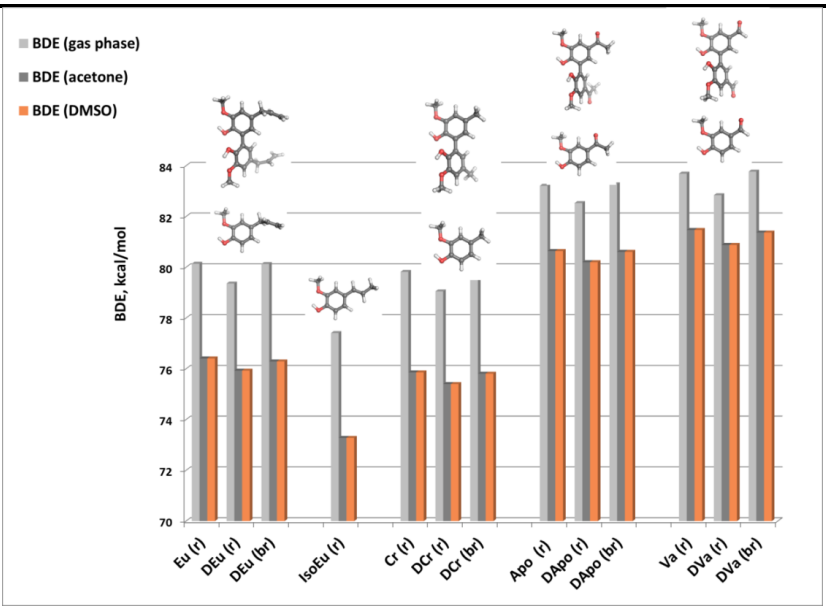

Figure 5. BDEs (in kcal/mol) in gas phase (light grey), acetone (grey) and DMSO (orange).

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АНТИОКСИДАНТНА АКТИВНОСТ НА ПОДБРАНИ *О*-МЕТОКСИФЕНОЛИ И БИФЕНОЛИ: ТЕОРЕТИЧНО И ЕКСПЕРИМЕНТАЛНО ИЗСЛЕДВАНЕ

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(Резюме)

Използвана е комбинация от теоретични и експериментални подходи за изследване и обяснение на зависимостта структура - антиоксидантна активност за избрани *орто*-метоксифеноли (природни и синтетични аналози). Съответните им димери (бифеноли) с гваяколови фрагменти са така подбрани, че да може се изследва влиянието на конформацията и заместителите в ароматния пръстен върху антиоксидантната активност. Антиоксидантната активност на изследваните съединения е определена от кинетичните криви на липидно автоокисление в хомогенна среда. На B3LYP/6-31+G** теоретично ниво са оптимизирани геометриите на всички молекули на изследваните съединения и на съответните им феноксилни радикали. Постигната е добра корелация между експериментално определената и теоретично предвидената активности, което е предпоставка за обяснение на зависимостта структура-активност.