Free Radical Research, 2002 Vol. 36 (8), pp. 859–867

Taylor & Francis
healthsciences

Quinones as Free-radical Fragmentation Inhibitors in Biologically Important Molecules

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Accepted by Professor L.J. Marnett

(Received 13 November 2001; In revised form 31 January 2002)

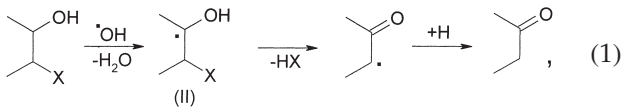
Effects of a number of quinones and diphenols of various structures on free-radical fragmentation processes taking place in α-diols, glycerol, 2-aminoethanol, glycero-1-phosphate, ethylene glycol monobutyrate, maltose, and some lipids were investigated. Quinone additions have been found to change the direction of free-radical transformations of the compounds cited above by inhibiting formation of the respective fragmentation products owing to oxidation of radicals of the starting compounds. The results obtained and literature data available allow a suggestion to be made that the system quinone/diphenol is able to not only deactivate or generate such active species as $O_2^{\bullet -}$ but also control the realization probability of free-radical processes of peroxidation and fragmentation in biologically important molecules.

Keywords: Radical; Fragmentation; Oxidation; Damage; Quinones; Diphenols

INTRODUCTION

When added to biologically important molecules, free-radical reaction initiators provoke a variety of homolytic processes therein.[1,2] Of such processes, the most studied are oxidation reactions of organic molecules, and, in the first place, the reactions of lipid peroxidation (LPO) taking place in the cell membranes. Activation of such reactions was shown to cause a large number of human diseases. Therefore, regularities in the LPO processes remain to be the subject of investigation in many scientific centers worldwide.

One of the most important results of these investigations is the finding that phenolic compounds are, as a rule, efficient inhibitors of peroxidation processes. The capability of phenol derivatives to slow down oxidation processes is due to their disposition to interact with reactive oxygen-centered radicals giving the resonance-stabilized phenoxy-radicals. In many respects, the anti-oxidative properties of certain phenol derivatives are the main factors determining the possibility of using them for prevention and treatment of diseases caused or accompanied by the LPO activation. Detailed information about the LPO processes, their role in biosystem damage, and anti-oxidant protection of an organism is contained in a comprehensive monograph,[3] and the literature cited therein. Under the action of ionizing radiation, light, peroxides, etc. on biosystems, realization of other processes, besides the LPO, is also possible. So, data have been reported[4–8] providing evidence that, in the course of reactions with free radicals, bifunctional organic compounds can undergo fragmentation according to the following general scheme:



(1)

where X = OH, NH_2, NHR, OR, OAc, OPO_3H_2.

The type (1) processes prevail in homolytic transformations of α-diols and the respective esters

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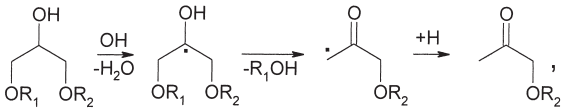
ISSN 1071-5762 print/ISSN 1029-2470 online © 2002 Taylor & Francis Ltd
DOI: 10.1080/1071576021000005294

and ethers, amino alcohols, amino acids, hydroxy aldehydes, etc. A key stage in these processes is the decomposition of radicals (II) that proceeds on account of rupture of two bonds in β-position to the radical center. In publications,[2,9–15] data pointing to the importance of type (1) processes are presented, exemplified by free-radical transformations of monosugars and polysaccharides,[9–12] amino acids and peptides,[2,13] and nucleosides.[14,15]

While studying properties of various glyceride radicals, generated either selectively[16] or under γ-irradiation of the starting systems,[17] we have demonstrated the possibility of the following fragmentation reaction to proceed in glycerophospholipids:



(2)

where $R_1 = -{}^{-}O(O)POCH_2CH_2N^{+}(CH_3)_3$, $R_2 = -COC_{15}H_{31}$ for lysophosphatidyl choline (LPC); $R_1 = -{}^{-}O(O)POCH_2CH(OCOC_{15}H_{31})CH_2OCOC_{15}H_{31}$, $R_2 = H$ for dipalmitoylphosphatidyl glycerol (DPPG).

In the course of free-radical transformations of sphingolipids, owing to a process similar to (2), fatty acid amides are formed.[18] Features of the damage caused to cell membrane components by free-radical fragmentation processes and biochemical consequences of the latter, are discussed in the literature.[19,20]

The data presented above point to the circumstance that the action on biosystems of free-radical reaction initiators can be realized through not only oxidation processes but through fragmentation reactions as well. Taking into account this established fact, the importance of the search for compounds that would be able to provide an efficient control over the realization probability of free-radical fragmentation processes taking place in biologically important substances becomes evident. This was the subject of the present work.

MATERIALS AND METHODS

Chemicals

The following compounds were used in the work: ethylene glycol, propylene glycol, and maltose from Aldrich; 2,3-butanediol, LPC, DPPG, dimyristoylphosphatidyl glycerol (DMPG), 5-methyl-2,3-dimethoxy-1,4-benzoquinone/ubiquinone Q_0/, and glycero-1-phosphate from Sigma; glycerol and 2-aminoethanol from Fluka. Monobutyrate of ethylene glycol was synthesized by esterification of ethylene glycol with butyric acid followed by isolation of the target product by column chromatography (hexane–ethyl acetate) on silica gel. The target product content, as determined by GLC, was 95%. The structure was confirmed by ^1H and ^{13}C NMR.

Hydroquinone, *p*-benzoquinone, pyrocatechol, 2-methyl-1,4-naphtoquinone and 2,3,5-trimethylhydroquinone from Aldrich were purified by recrystallization, vacuum sublimation, and column chromatography. Physico-chemical and spectral characteristics of the purified samples comply with the literature data.

2,5-Di-*tert*-butylhydroquinone,[21] as well as 4-*tert*-butyl- and 3,5-di-*tert*-butylpyrocatechols,[22] have been synthesized by alkylation reactions of hydroquinone or pyrocatechol, respectively, with *tert*-butyl alcohol in the presence of sulphuric or perchloric acid. Controlled oxidation of the respective hydroquinone or pyrocatechol derivatives followed by isolation and purification of the target products yielded 2,3,5-trimethyl- and 2,5-di-*tert*-butylbenzoquinones-1,4,[23] 4-*tert*-butyl- and 3,5-di-*tert*-butylbenzoquinones-1,2.[24] Physico-chemical and spectral characteristics of the prepared compounds have been determined, and their composition and structures have been reliably established by elemental analysis, IR, UV, ^1H NMR and mass spectrometry.

Preparation of Solutions

Distilled water was used for preparation of 0.1 M solutions of the compounds under study. The necessary pH 6.8–6.9 of 2-aminoethanol solutions was achieved by adding aqueous perchloric acid solution. Solutions containing diphenols or quinones were prepared by dissolving the appropriate weighed amounts of the latter in a solution of the respective compound studied. Concentrations of phenols or quinones were generally 10^{-3} M. Concentration of solutions of 2-methyl-naphtoquinone-1,4 was 7.5×10^{-4} M because of limited solubility of this compound in water. Maltose solutions contained 10^{-2} M of diphenol or quinone.

Preparation of Liposomes

Multilamellar liposomes were prepared using the thin film hydration method.[25] A lipid solution in chloroform, with or without addition of a diphenol or quinone, was evaporated in a rotary evaporator and kept under vacuum for at least 1 h to remove traces of solvent. To the lipid film thus formed, an appropriate quantity of 0.15 M NaCl solution was added, and all this was homogenized at 37°C using a Vortex mixer. Phospholipid concentration in the liposome suspension was 0.02 M; diphenol or quinone concentration was 2×10^{-4} M.

Radiation Experiments

Initiation of free-radical transformations was performed by exposing the initial samples to γ-radiation. The solutions under study were transferred to glass ampoules, blown through with an inert gas (high purity argon) for 40–60 min to remove dissolved oxygen, sealed, and irradiated in a γ-ray installation equipped with a ^{137}Cs source. Absorbed dose rate provided by the γ-ray installation was 0.33 ± 0.01 Gy/s, and the range of doses absorbed used in the study was 0.2–4 kGy. Aqueous maltose solutions were irradiated in the range of 1–20 kGy.

Determination of Molecular Products of Radical Transformations

To determine reaction products formed in the course of free-radical fragmentation, various chromatographic methods were used.

Analysis of products of free-radical transformations of α-diols (ethanal, propanal, acetone, 2-butanone, 2-hydroxyethanal, 1-hydroxy-2-propanone, 3-hydroxy-2-butanone) was performed by gas chromatography using a quartz capillary column HP-Wax (30 m length, 0.53 mm ID, 1 μm df). Chromatographic conditions: starting temperature 60°C; temperature increase rate 8°C/min up to 140°C; flame ionization detector.

The analyses for 1-hydroxy-2-propanone in glycerol or glycero-1-phosphate solutions, 1-palmitoxy-2-propanone and butyric acid, were performed using a capillary column Stabilwax-DA (10 m length, 0.53 mm ID, 1 μm df), Restek. Chromatographic conditions: isothermal mode of operation; temperature 90°C (for 1-hydroxy-2-propanone), or 200°C (for 1-palmitoxy-2-propanone), or 105°C (for butyric acid); flame ionization detector.

Ammonia in 2-aminoethanol solutions was determined using an amino-acid analyzer T339 (Mikrotechna, Praha) with a column (36 cm length, 0.37 cm ID) filled with a strongly acid sulphopolystyrene cation exchanger of Aminex A-5 brand (grain size 13 ± 2 μm). The column temperature was 70 ± 1°C; eluent was Na-citrate buffer pH 9.95. Ten-fold dilutions of the samples were made before analysis.

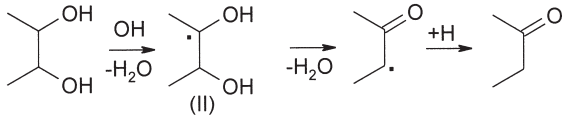
Method of quantitative determination of D-glucose in γ-irradiated maltose solutions included separation on a silica gel layer using "Sorbfil" plates free of organic binding material. Before the analysis, a preliminary full-height elution of the plates with the solvent to be used (acetonitrile/water, 85:15 v/v) was performed, followed by thermal activation at 100 ± 5°C for 60 min. The separation was conducted in a chamber for ascending chromatography. To achieve a better separation, thrice-repeated elution with the solvent was performed. Visualization of the sugar spots was obtained by spraying with a solution of aniline–diphenylamine–85% phosphoric acid mixture in acetone followed by development at 100 ± 5°C for 15 min. The quantitative determination of D-glucose was performed spectrophotometrically, after extraction with acetone of the colored product formed after reaction of glucose with the visualizing reagent (absorption maximum at 630 nm).

Phosphatidic acid (PA) was determined by thin-layer chromatography. Lipids from the samples were extracted by shaking the respective aqueous suspensions with two-fold quantities of chloroform–methanol mixture (2:1, v/v). After separation of layers by centrifugation, the lower layer was concentrated and applied on TLC plates (0.2 mm silica gel, Aldrich). The plates were developed in the solvent system $CHCl_3/CH_3OH/NH_4OH$ (13:5:1, v/v/v). The respective lipid spots were scratched out, and the concentration was further determined according to the method described in Ref. [26]. Analysis of inorganic phosphate in γ-irradiated solutions of glycero-1-phosphate was carried out according to Ref. [27].

RESULTS

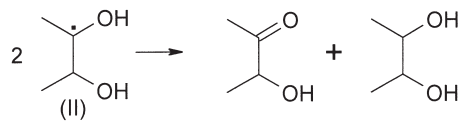
Quinones as Inhibitors of Homolytic Dehydration of α-diols and Glycerol

For the first time, the possibility of radical fragmentation with rupture of two bonds has been demonstrated using α-diols as example.[4–7] It has been found that such agents as Fenton's reagent, γ-radiation, and others, initiate dehydration of α-diols that proceeds according to the following scheme:



(3)

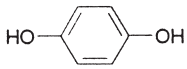
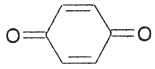
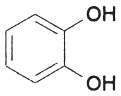
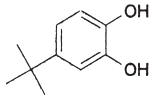
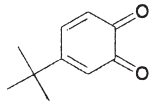
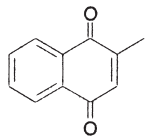
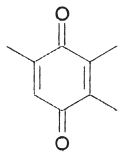
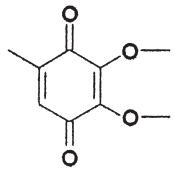
Influence of various factors on realization probability of the process (3) was studied, and details of the dehydration mechanism of α-diol radicals (II) were scrutinized.[6,7] In the course of hemolytic transformations of α-diols, besides dehydration products, oxidation products of the initial compounds are formed, due to bimolecular process of disproportionation of the radicals (II).[28]



(4)

In the present work it was shown that quinones added to α-diol solutions cause sharp changes

TABLE I Product yields obtained on γ-radiolysis of 0.1 M aqueous solutions of butanediol-2,3 in the presence of diphenols and quinones of various structure

Additives	C, M	G (product) × 10^7 (mol/J)	
		2-Butanone	3-Hydroxy-2-butanone
No addition	–	1.02 ± 0.02	0.28 ± 0.01
Hydroquinone 	10^{-3}	0.82 ± 0.06	0.23 ± 0.05
Benzoquinone-1,4 	10^{-3}	0	3.1 ± 0.4
Pyrocatechol 	2×10^{-3}	1.91 ± 0.05	0.62 ± 0.12
4-*tert*-Butylpyrocatechol 	10^{-3}	1.40 ± 0.05	0.63 ± 0.07
4-*tert*-Butylbenzoquinone-1,2 	10^{-3}	0.04 ± 0.01	1.92 ± 0.09
2-Methylnaphtoquinone-1,4, (Menadione, Vitamine K_3) 	7.5×10^{-4}	0.18 ± 0.04	2.5 ± 0.6
2,3,5-Trimethyl-benzoquinone-1,4 	10^{-3}	0.37 ± 0.16	2.6 ± 1.1
5-Methyl-2,3-dimethoxybenzoquinone-1,4 (Ubiqinone Q_0) 	10^{-3}	0.04 ± 0.01	2.2 ± 0.6
Oxygen, O_2	$\sim 2.7 \times 10^{-4}$	0.16 ± 0.02	3.3 ± 0.4

in the dehydration/oxidation product ratio of the latter. So, in radiolysis of 2,3-butanediol aqueous solutions, various quinones provoke a sharp fall in 2-butanone yield, and a simultaneous yield increase for 3-hydroxy-2-butanone—an oxidation product (see Table I). Unlike quinones, diphenols and their derivatives did not produce such changes (Table I). We have observed similar effects also on radiolysis of aqueous solutions of other vicinal diols and glycerol. This is exemplified by the data presented in Table II concerning effects of ubiquinone Q_0 on radiolysis of aqueous solutions of ethylene glycol and 1,2-propanediol, and in Table III concerning effects of some quinones and *tert*-butylated pyrocatechol on radiolysis of aqueous glycerol solutions.

Dehydration processes of type (3) take place when free-radical reaction initiators act on biologically important substances such as carbohydrates,[2,9,12,29] nucleosides,[15,30] and 5′-nucleotides.[30] In the last case, transformation of RNA nucleotides in DNA nucleotides occurs. The possibility of regulating this process by means of biologically active quinones appears to be of considerable interest for biochemists.

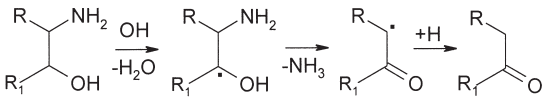
Quinones as Inhibitors of Homolytic Deamination Processes

In the course of hemolytic transformations of amino alcohols[31–33] and hydroxyl-containing amino acids,[34] deamination processes occur,

TABLE II Effects of ubiquinone (Q_0) on radiolysis product yields in deaerated 0.1 M aqueous solutions of ethylene glycol and 1,2-propanediol

Compounds studied	Products	G (product) $\times 10^7$ (mol/J)	
		Without additives	In the presence of ubiquinone (Q_0), 10^{-3} M
Ethylene glycol	Ethanal	1.64 ± 0.34	0.04 ± 0.01
	2-Hydroxyethanal	0.25 ± 0.11	3.8 ± 1.1
1,2-Propanediol	2-Propanone	1.74 ± 0.20	0.03 ± 0.01
	1-Hydroxy-2-propanone	1.04 ± 0.13	4.9 ± 1.1

where fragmentation of radicals formed from the initial compounds plays an essential role (5):



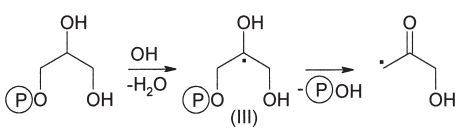
(5)

where $R, R_1 = H$, Alk are amino alcohols; R = COOH, $R_1 = H$ is serine, $R_1 = CH_3$ is threonine.

Realization probability and mechanism of the deamination process are substantially dependent on the form in which the amino-containing compounds are present in aqueous solutions.[33,34] In neutral aqueous solutions of 2-amino ethanol, where the amino group is protonated, the deamination proceeds mainly owing to fragmentation of a zwitterionic form ($^+NH_3CH_2C^{\bullet}HO^-$) of amino alcohol radicals. Quinone additions into 2-amino ethanol solutions decrease sharply the deamination product yields in neutral media (see Table III), and hence, they suppress fragmentation processes of the respective radicals. In the presence of oxygen, the deamination process of 2-amino-ethanol is suppressed to a lesser extent than in the presence of quinones. So, the yields of ammonia and ethanal on irradiation of 2-amino ethanol solutions in the presence of oxygen are $(1.71 \pm 0.12) \times 10^{-7}$ and $(0.13 \pm 0.014) \times 10^{-7}$ mol/J, respectively.

Suppression of Homolytic Deesterification Processes of Glycerol Esters by Quinones

Free-radical transformations of glycerophosphates were the subject of detailed investigations, because regularities of phosphoester bond cleavage under the action of active radical species on polynucleotides, glycerophospholipids, etc. were studied using these model objects.[35–38] The elimination of inorganic phosphate was shown to proceed according to the following scheme:



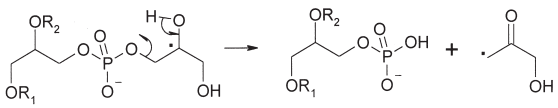
(6)

P = $-PO_2H_2$

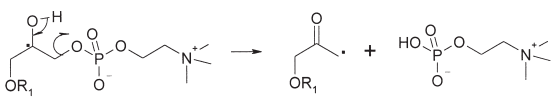
Quantitative formation, with a rate constant of $> 10^6\,s^{-1}$, of phosphate anions from the radicals (III) was observed. A detailed kinetic study of phosphate anion elimination from organic radicals is described in Ref. [39].

We have found that additions of 4-*tert*-butylbenzoquinone-1,2 to glycero-1-phosphate solutions decrease the inorganic phosphate yields by a factor of 2 (see Table III). A similar effect was observed in radiolysis of aqueous solutions of ethylene glycol monobutyrate. So, the yield of butyric acid on radiolysis of 1×10^{-2} M solution of the latter is $(2.41 \pm 0.70) \times 10^{-7}$ mol/J, and it falls down to $(0.59 \pm 0.03) \times 10^{-7}$ mol/J after introduction of 10^{-3} M of 4-*tert*-butylbenzoquinone-1,2 into the solution (see Table III). It has been shown[40,41] that radicals of α-diol esters decompose at a high rate. Nevertheless, as it follows from the data presented above, quinone additives inhibit this process.

Taking into account the fact that quinones inhibit fragmentation processes of ester radicals in aqueous solutions, evaluation of probability of such effects to occur in homolytic transformations of lipids appeared to be of interest. For this purpose, investigations of influence of di-*tert*-butylated derivatives of 1,2- and 1,4-quinones on radiation-induced free-radical fragmentation of DPPG, DMPG, and LPC were performed. The main molecular fragmentation product of DPPG and DMPG is PA, and the carbonyl-containing fragmentation product is 3-hydroxy-2-propanone (reaction (7)). In the case of LPC, the main carbonyl-containing fragmentation product is 1-palmitoxy-2-propanone (reaction (8)).



(7)



(8)

where $R_1 = R_2 = CO(CH_2)_{14}CH_3$ for DPPG and LPC; $R_1 = R_2 = CO(CH_2)_{12}CH_3$ for DMPG.

Data about the effects of various quinones on radiation-chemical yields of PA, 1-hydroxy-2-propanone and 1-palmitoxy-2-propanone are presented in Table IV. In the cases of both micellar solutions of LPC and multilamellar liposomes of dipalmitoyl- or dimyristoyl phosphatidyl glycerol, a decrease

TABLE III Effects of quinones and diphenols on radiolysis product yields in deaerated aqueous solutions of glycerol, 2-aminoethanol, glycero-1-phosphate, maltose (0.1 M) and 2-butyroxyethanol (0.01 M)

Compounds studied	Products	G (product) × 10^7(mol/J)						
		Without additives	Hydroquinone, 10^{-3} M	4-*tert*-Butyl-pyrocatechol, 10^{-3} M	1,4-Benzoquinone, 10^{-3} M	4-*tert*-Butyl-1, 2-benzoquinone, 10^{-3} M	2-Methyl-1, 4-naphtoquinone, 7.5×10^{-4} M
Glycerol	1-Hydroxy-2-propanone	0.47 ± 0.08	0.59 ± 0.08	0.46 ± 0.08	0	0	0.12 ± 0.02
2-Aminoethanol	Ammonia	3.44 ± 0.05	–	–	096 ± 0.03	096 ± 0.03	0.75 ± 0.42
	Ethanal	0.73 ± 0.02			0	0	0
Glycero-1-phosphate	Phosphate-anion	3.67 ± 0.21	–	–	–	1.67 ± 0.05	2.2 ± 0.3
2-Butyroxyethanol	Butyric acid	2.41 ± 0.70	–	2.46 ± 0.38	–	0.59 ± 0.03	–
	Ethanal	0.51 ± 0.07	–	0.59 ± 0.07	–	0.02 ± 0.01	–
Maltose	D-Glucose	1.14 ± 0.17	0.93 ± 0.08	1.04 ± 0.11	0.37 ± 0.12	0.39 ± 0.07	–

in fragmentation product yields is observed in the presence of the quinones studied.

Effect of Quinones on Homolytic Cleavage of *O*-glycoside Bond

It is known that, under the action of radiation or other free-radical reaction initiators on solutions of di- and polysaccharides, products with smaller molecular mass than that of initial compounds are formed. Evidence of a significant contribution of the fragmentation reaction of type (1) to the radical-induced destruction of carbohydrates is given in publications.[10,11] This process can be described as follows:

(9)

We have shown that 1,2- and 1,4-quinones lower efficiently the yields of D-glucose formed on radiolysis of aqueous solutions of maltose, whereas the respective reduced forms—hydroquinones—have virtually no effect on this process (see Table III).

DISCUSSION

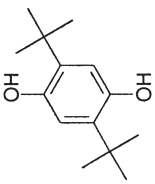
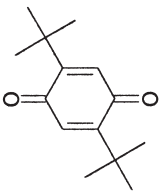
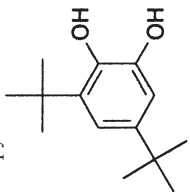
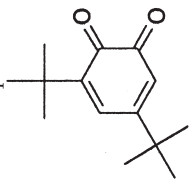
For better understanding the essence of these phenomena, namely that quinones are efficient inhibitors of free-radical fragmentation reactions of organic substances, let us consider various ways of affecting the realization probability of the type (1) processes by quinones. This influence can be exerted in the initiation stage, because quinones are known to be efficient acceptors of OH radicals.[42] The hydroxylation reaction of benzoquinone (10)

(10)

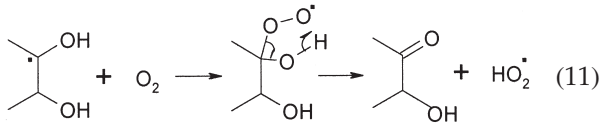
proceeds with a rate constant of $K_{10} = 6.6 \times 10^9\,M^{-1}\,s^{-1}$. In our case, the $^{\bullet}OH$ radical capture owing to the reaction (10) can make at most 3%, because concentration ratio of the main substance to diphenol or quinone additives is ≥100 in the systems studied, while the reaction of $^{\bullet}OH$ radicals with the substrate has the rate constant of the order of $\sim 2 \times 10^9\,M^{-1}\,s^{-1}$.[43] Taking this into account, the reaction (10) will not play a determining role in inhibition by quinones of fragmentation product formation from the substances studied.

In the article,[8] data are presented pointing to an efficient role of molecular oxygen and ions of variable valency, such as Cu^{2+} ions, as fragmentation

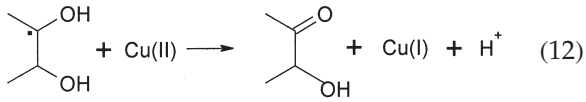
TABLE IV Product yields on radiolysis of aqueous suspensions of lipids (0.02 M) in the absence and in the presence of diphenols (2×10^{-4} M) and quinones (2×10^{-4} M) of various structures

Compounds studied	Products	G (product) $\times 10^7$ (mol/J)				
		Without additives	2,5-di-*tert*-Butyl-hydroquinone 	2,5-di-*tert*-Butyl-1,4-benzoquinone 	3,5-di-*tert*-Butyl-pyrocatechol 	3,5-di-*tert*-Butyl-1,2-benzoquinone 
Dipalmitoylphosphatidyl glycerol	Phosphatidic acid	1.17 ± 0.11	0.80 ± 0.08	0.57 ± 0.10	1.10 ± 0.11	0.80 ± 0.08
	Hydroxyacetone	0.24 ± 0.02	0.17 ± 0.02	0.13 ± 0.02	0.19 ± 0.02	0.15 ± 0.03
Dimyristoylphosphatidyl glycerol	Phosphatidic acid	1.46 ± 0.25	1.36 ± 0.24	0.85 ± 0.22	–	–
	Hydroxyacetone	0.23 ± 0.15	0.12 ± 0.02	0.16 ± 0.03	–	–
Palmitoylisophosphatidyl choline	Palmitoxyacetone	1.10 ± 0.16	0.77 ± 0.16	0.43 ± 0.08	–	–

reaction inhibitors of α-diol radicals. In the presence of O_2 and Cu^{2+}, oxidation of the α-diol radicals to the respective carbonyl compounds takes place:

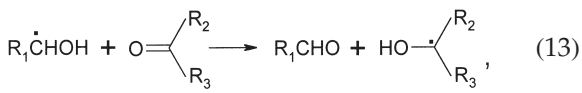

(11)

(III)

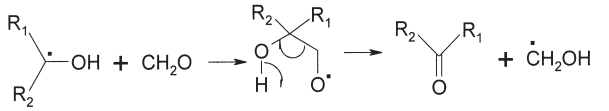

(12)

The oxidation by oxygen of α-hydroxyalkyl radicals involves an addition stage followed by disintegration of the radicals (III) via a five-membered transition state.[2,8]

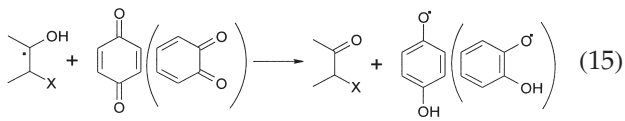
While studying transformations of alcohol radicals in the presence of aldehydes and ketones, the carbonyl-containing compounds were found to be also capable of oxidizing α-hydroxyalkyl radicals:


(13)

In the case of formaldehyde, as in the case of oxygen, this process involves an addition stage followed by decomposition of the radical adduct formed:[8]

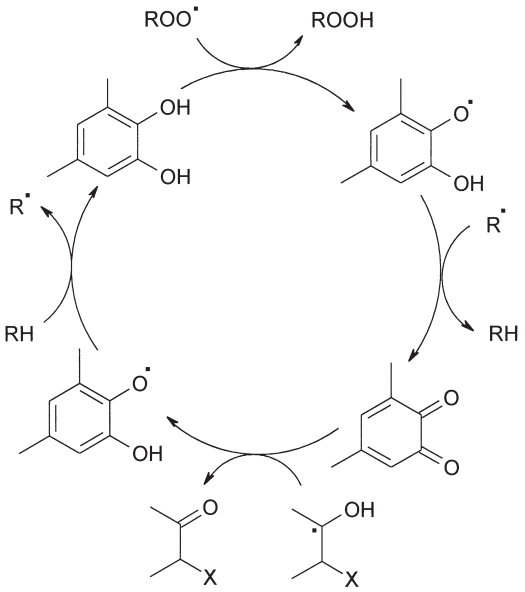

(14)

Based on the facts indicated above and results obtained, we believe that the suppression of fragmentation reaction of organic compounds (1) by quinones is possible owing to the following process:


(15)

As a result of the reaction (15), a decrease in yields of fragmentation products of the initial compounds and an increase in yields of the respective oxidation products should be observed, and indeed, this is confirmed experimentally (see Tables I and II). Some mechanistic details of the reaction (15) still have to be elucidated, namely whether oxidation of α-hydroxyl radicals by quinones takes place via addition and decomposition stages (similar to reactions (11) and (14)), or by means of an H-atom transfer, or as a result of a consecutive transfer of e^- and H^+.

The finding that quinones are capable of suppressing the fragmentation reaction (1) opens up



SCHEME 1 Scheme of a possible reaction cycle for suppression of free-radical oxidation and fragmentation processes by diphenol derivatives.

interesting prospects regarding the search for substances that would inhibit various types of free-radical processes. In our opinion, the use of hydroquinone and pyrocatechol derivatives for solving such problems appears to be the most promising. In the presence of oxygen in biosystems, these compounds will play the role of antioxidants. While suppressing peroxidation processes, they are oxidized into the respective quinones, which are able to inhibit fragmentation reactions. In other words, for the suppression of various free-radical processes to occur, the substances used should inhibit peroxidation processes in their reduced form, while inhibiting fragmentation processes in their oxidized form, i.e. they should provide realization of the following reaction cycle (see Scheme 1).

Thus, it has been shown in the course of the studies performed that quinone derivatives are capable of inhibiting free-radical fragmentation reactions which play an essential role in the damage of biologically important molecules. The results obtained, as well as the literature data available,[3] enabled us to suggest that the system diphenol/quinone is able to not only deactivate or generate such radical species as superoxide radical-anion ($O_2^{\bullet -}$) but also control the realization probability of free-radical processes of peroxidation and fragmentation of biologically important substances.

Acknowledgements

This work was supported by the International Science and Technology Centre (Grant # B-434).

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