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Interaction of Hydroxyaryl Aldehydes with α-Hydroxyethyl Radicals

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Abstract—The effect of some hydroxylated aromatic aldehydes on the radiation-chemical transformations of deaerated ethanol during continuous radiolysis has been studied. The data obtained show that these compounds effectively inhibit radiation-induced processes involving α-hydroxyethyl radicals (α-HER). Benzaldehyde and its hydroxylated derivatives (II, III) predominantly oxidize, and compounds containing the cinnamic moiety, (IV–VI), add α-HER to a carbonyl group or –C=C bond.

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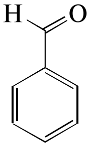
Hydroxylated aromatic aldehydes (hydroxyarene carbaldehydes) refer to the numerous class of plant phenols. Exhibiting antioxidant properties, they are able to regulate free radical processes in biological systems and, as such, have useful medical properties [1]. Plant phenols also exhibit radioprotective properties due to the inhibition of radiation-induced free radical oxidation and degradation of vital components of living organisms [2]. The antioxidant properties of phenolic compounds are generally related to their ability to reduce the peroxyl radicals ($ROO^\bullet$) resulting from the action of radiation or free radical agents on organic compounds in the presence of oxygen. Satisfactory correlations between the reducing properties depending on the –O–H bond strength of phenols and their antioxidant activity were obtained [3, 4].

In our studies we have shown that the fragmentation reactions, proceeding through the stage of the formation and subsequent decay of α-hydroxylated carbon-centered radicals of parent compounds, make a considerable contribution to the radiation-induced transformations of hydroxyl-containing compounds, such as lipids, carbohydrates, and peptides [5–7]. It has been established that these processes are inhibited by quinones and other carbonyl compounds [8–10]. It is unknown whether hydroxylated aromatic aldehydes can interact with α-hydroxylated carbon-centered radicals and block the fragmentation or not. Such information can be obtained by studying the effect of hydroxyaryl aldehydes on the formation of final products of radiolysis of deaerated ethanol, which yields α-hydroxyethyl radicals (**α-HER**) during its γ-irradiation.

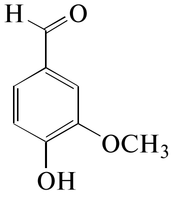
Studying the reactions of hydroxylated aromatic aldehydes with α-HER is of interest partly due to the necessity of evaluation of hepatoprotective properties of these compounds, since the cytotoxic and mutagenic properties of ethanol are largely related to the α-HER formation during its metabolic conversion in human liver by the action of cytochrome P_{450} [11], with the degree of damage to biomolecules being directly dependent on the concentration of natural scavengers of radical intermediates [12]. A number of alcoholic beverages that are produced through long-term storage in oak barrels as a manufacturing technology step accumulate significant amounts of hydroxylated derivatives of cinnamaldehyde and benzaldehyde as a result of the lignin ethanolysis and hydrolysis processes [13].

EXPERIMENTAL

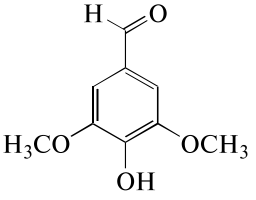
4-Hydroxy-3-methoxybenzaldehyde (II), 4-hydroxy-3,5-dimethoxybenzaldehyde (III), *trans*-cinnamaldehyde or cinnamaldehyde (IV), *trans*-4-hydroxy-3-methoxycinnamaldehyde (V), *trans*-4-hydroxy-3,5-dimethoxycinnamaldehyde (VI), acetaldehyde (AA), and (+/-)-*meso*-2,3-butanediol (2,3-BD) (Sigma Aldrich) and 2-methoxyphenol (VII) (Fluka) were used without further purification. Benzaldehyde (I) was distilled at 10 mmHg before using. Rectified ethanol (96 vol %) was purified by sorption on Wolfen Zeosorb LA zeolite followed by fractional distillation.



(I)



(II)



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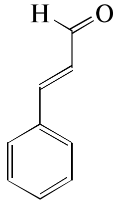

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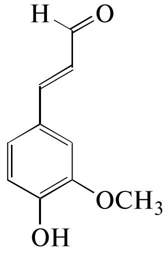
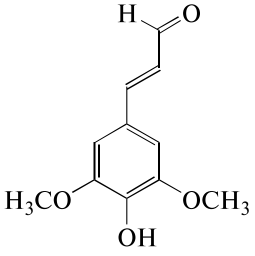
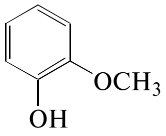


(V)



(VI)



(VII)

Solutions of test compounds were prepared by dissolving their weighed portions in ethanol. Because of the solvent high volatility, oxygen removal and sealing of ampoules with deaerated solutions were carried out as described in [14]. Irradiation was performed on a MPX-γ-25M facility with a ^{60}Co source. The absorbed dose rate was 0.45 ± 0.005 Gy/s, and the absorbed dose range was 0.27–1.35 kGy.

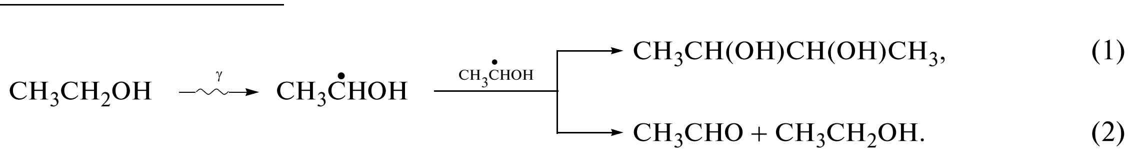
Acetaldehyde and 2,3-butanediol were determined by gas–liquid chromatography on a Shimadzu GC-17A instrument with a flame-ionization detector and a RTX-WAX capillary column (length 30 m, inner diameter 0.32 mm, stationary-phase film thickness 0.5 μm). The analysis conditions were as follows: carrier gas, nitrogen; column oven program, heating from 40 to 200°C with a gradient of 13°C/min; and superficial gas velocity in the column, 0.25 m/s. The injector and detector temperatures were 220°C. The concentrations of hydroxyaryl aldehydes in the initial and irradiated solutions were determined by gas–liquid chromatography on the Shimadzu GC-17A with a RTX-1 capillary column (length 30 m, inner diameter 0.32 mm, stationary-phase film thickness 0.5 μm). The analysis conditions: carrier gas, nitrogen; column oven program, heating from 60 to 290°C at a rate of 8°C/min and volumetric gas flow rate in the column, 4 ml/min. The injector and detector temperatures were 270°C. The substances were identified by their retention times relative to standards; the concentrations were calculated using calibration coefficients.

Molecular products of α-HER reactions with the test compounds were identified by gas chromatography using a Shimadzu GCMS-QP2010 Plus mass-selective detector with a Equity-5 column (length 30 m, inner diameter 0.25 mm, stationary-phase thickness 0.25 μm). The analysis conditions: carrier gas, helium; superficial gas velocity in the column, 0.365 m/s; column oven program, heating from 60 to 270°C at a rate of 5°C/min; injector temperature, 270°C; ion source and interface temperatures, 280°C.

The radiation-chemical yields of radiolysis products and solute consumption were calculated from the linear portions of concentration versus absorbed dose curves by the least squares technique.

RESULTS AND DISCUSSION

The radiation-chemical transformations of ethanol have been studied in detail [15]. The main molecular products of the radiolysis of deaerated ethanol in the absence of additives are 2,3-BD and AA, which are predominantly generated the in equiprobable combination (1) and disproportionation (2) reactions of α-HER:



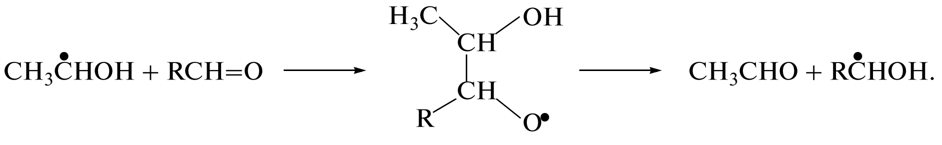
$$CH_3CH_2OH \xrightarrow{\gamma} CH_3\dot{C}HOH \xrightarrow{CH_3\dot{C}HOH} \begin{cases} CH_3CH(OH)CH(OH)CH_3, & (1) \\ CH_3CHO + CH_3CH_2OH. & (2) \end{cases}$$

For this reason, the comparison of the radiation-chemical yields of products of these reactions during the radiolysis of deaerated ethanol in the presence and absence of various additives makes it possible to determine the reactivity of the test compounds and the mechanism of their reaction with α-HER.

The radiation-chemical yields of the main products of deaerated-ethanol radiolysis in the presence of the test compounds are given in the table. These data indicate that the admixture of compounds I–VI changes the ratio between the main deaerated-ethanol radiolysis products in favor of AA. This fact demonstrates the ability of test compounds I–VI to oxidize the α-HER.

Notably, the AA and 2,3-BD radiation-chemical yields remain unchanged during the radiolysis of deaerated ethanol in the presence of guaiacol VII, as compared to the additive-free system, and the radiation-induced decomposition of the additive barely occurs. These findings show that guaiacol VII has low reactivity toward α-HER. Consequently, the aldehyde group, rather than the phenol moiety, in the structure of the test compounds is responsible for the effects observed during the radiolysis of deaerated ethanol in the presence of compounds I–VI.

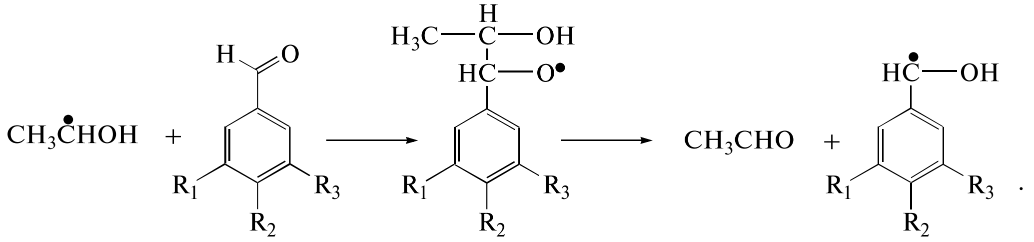
It has been shown that carbonyl compounds, such as aldehydes [16], quinones [8], and flavonoids [10], are able to efficiently oxidize hydroxyalkyl radicals. In the case of aliphatic aldehydes, it was proved that the α-HER oxidation reaction proceeds through the stage of radical addition to the carbonyl group yielding radical adduct VIII [16]:



(VIII)

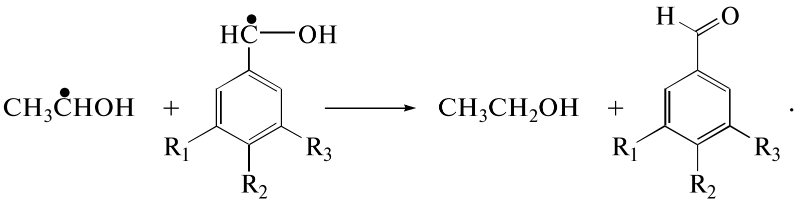
$$\mathrm{CH_3\dot{C}HOH + RCH{=}O \longrightarrow H_3C{-}CH(OH){-}CH(R){-}O^{\bullet} \longrightarrow CH_3CHO + R\dot{C}HOH.} \qquad (3)$$

In the case of compounds I–VI, the occurrence of a reaction of this type should lead to an increase in the AA formation and solute degradation radiation-chemical yields, which can be represented by the following scheme for benzaldehyde and its derivatives (II, III):



(4)

However, the data obtained (table) show that during the radiolysis of deaerated ethanol in the presence of compounds I–III, the decrement in the 2,3-BD is greater than the increment in the AA yield. In addition, relatively low decomposition yields are observed for these substances. This suggests the possibility of regeneration of the radicals, produced via reaction (4), back to the parent compounds through the following process:



(5)

The consecutive occurrence of reactions (4) and (5) results in a significant decrease in the 2,3-BD yield, an increase in AA yield, and the regeneration of compounds I–III.

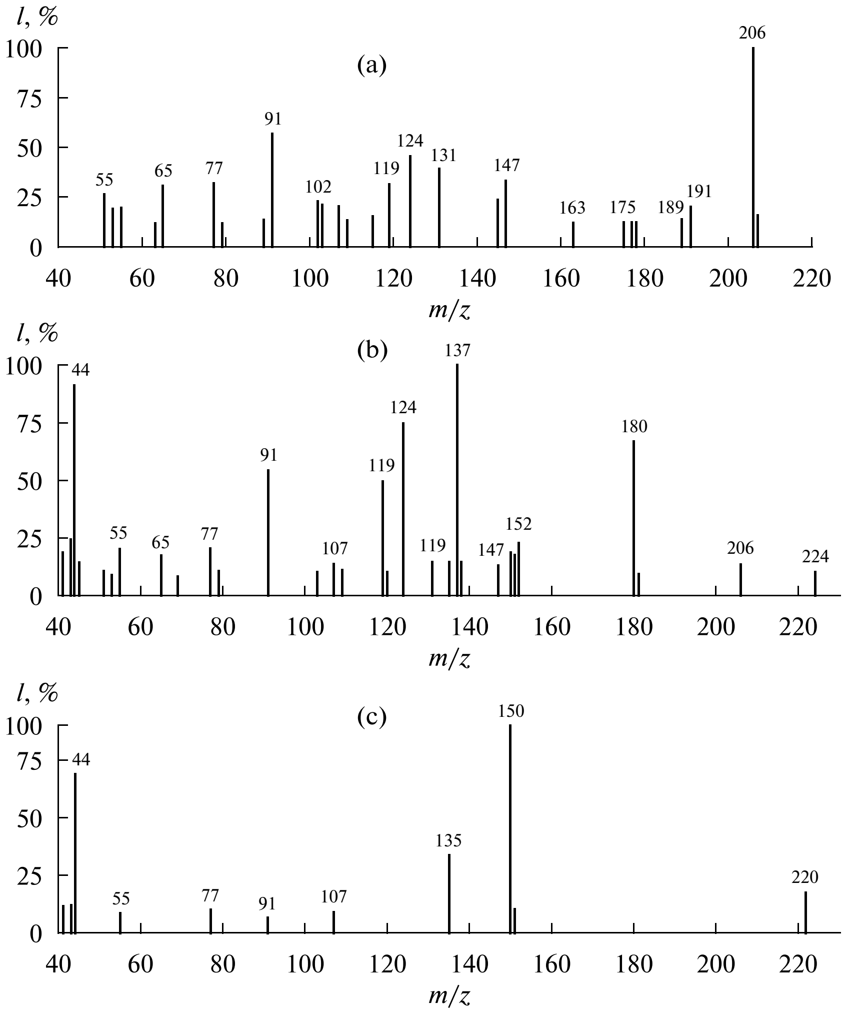
In the case of radiolysis of deaerated ethanol in the presence of cinnamic aldehyde and its derivatives V and VI, the yield of 2,3-BD considerable decreased and the radiation-induced decomposition of the addi-

Effect of hydroxyaryl aldehydes and 2-methoxyphenol on the radiation-chemical yields of the main radiolysis products of deaerated ethanol

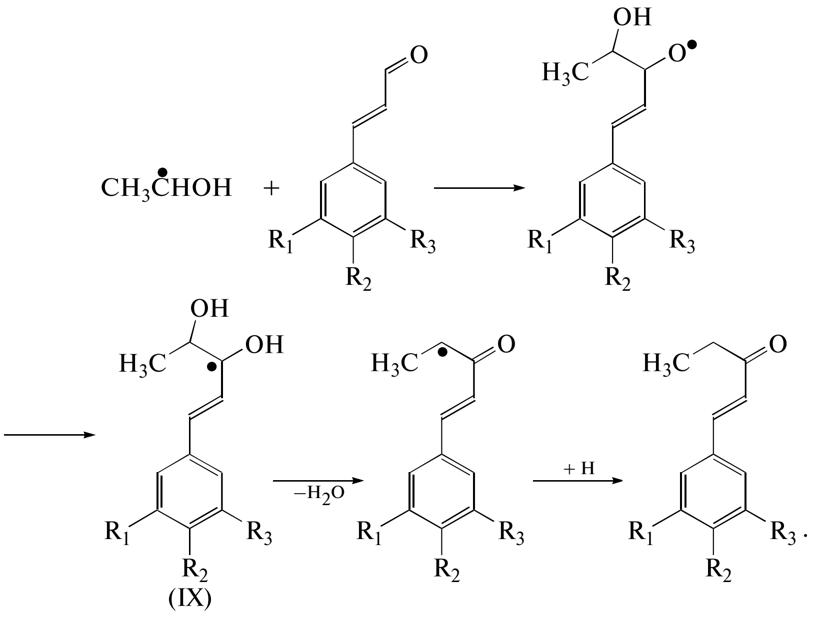
Additive, $c = 10^{-3}$ mol/l	Radiation-chemical yield (G), molecule/100 eV		
	acetaldehyde	2,3-butanediol	additive decomposition
Additive-free	1.60 ± 0.07	1.56 ± 0.03	–
I	2.37 ± 0.07	0.35 ± 0.01	–1.79 ± 0.07
II	2.06 ± 0.12	0.56 ± 0.04	–1.21 ± 0.08
III	2.25 ± 0.10	0.47 ± 0.03	–1.93 ± 0.10
IV	1.47 ± 0.06	0.02 ± 0.01	–4.28 ± 0.09
V	1.54 ± 0.18	0.07 ± 0.01	–4.45 ± 0.15
VI	1.63 ± 0.07	0.05 ± 0.02	–3.40 ± 0.11
VII	1.42 ± 0.06	1.51 ± 0.07	–0.07 ± 0.05

tives was significant; however, the AA yield remained almost unchanged as compared to that for the additive-free system. This difference of cinnamic compounds IV–VI from benzaldehyde and its derivatives II and III is an indication of the likelihood of additional mechanisms of interaction between α-HER and compounds containing the acrolein moiety.

We have identified the molecular products of radiolysis of compounds I–VI in deaerated ethanol by gas chromatography–mass spectrometry. The figure shows typical mass spectra of the major products of radiolysis of the cinnamic compounds. The main molecular products of radiolysis of compounds IV–VI are adducts with a molecular mass M greater than that of the parent compounds, $M = M_{(\text{additive})} + M_{(\text{ethanol})} - M_{(\text{water})}$ (figure, spectrum a). Based on the analysis of the mass spectra patterns for radiolysis products having the above-specified molecular masses, we have assumed that the identified substances are formed as the result of α-HER addition to the carbonyl group of compounds IV–VI followed by the dehydration of intermediate radical adducts IX according to the scheme:



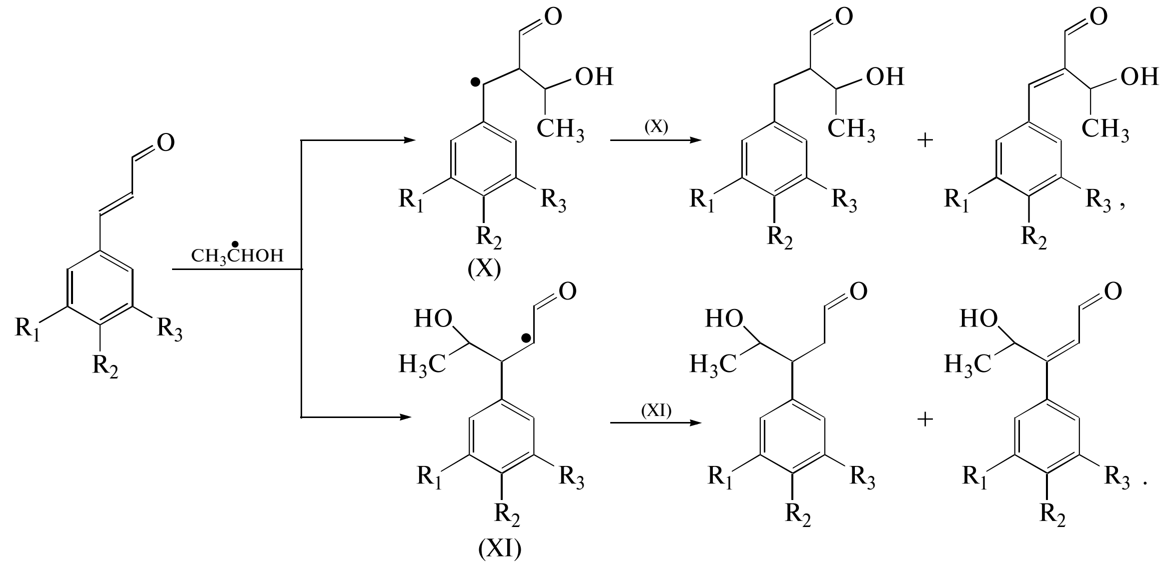
Mass spectra of the products of α-HER addition to (a) the C=O group and (b, c) the –C=C bond of 3-methoxy-4-hydroxycinnamaldehyde (IV).



(6)

The above mechanism of interaction with α-HER during the radiolysis of compounds IV–VI in deaerated ethanol can explain both the almost complete suppression of the radiation-chemical yield of 2,3-BD and high radiation-chemical yields for the decomposition of the test compounds.

Along with the α-HER adducts to the carbonyl group, a series of compounds with molecular masses of $M = M_{(\text{additive})} + M_{(\text{ethanol})}$ and $M = M_{(\text{additive})} + M_{(\text{ethanol})} - 2$ were identified as minor products of radiolysis of cinnamic aldehyde and its derivatives V and VI (figure; spectra b, c). This finding demonstrates that compounds of the cinnamic series are capable of addition of α-HER across the –C=C bond conjugated with the carbonyl group:



(7)

(8)

Comparing the data obtained in the deaerated-ethanol radiolysis study, we can conclude that the compounds examined effectively interact with α-hydroxyethyl radicals via different mechanisms. The ability of hydroxyaryl aldehydes to oxidize or attach alcohol radicals should be taken into account when they are used as modulators of free radical processes in human body, since they affect in different manners the yields of toxic products of free-radical transformations of alcohols.

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