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Dual Effect of Organomercury Compounds on Peroxide Oxidation of Oleic Acid

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Abstract — Oxidation of oleic acid with atmospheric oxygen in the presence of $HgCl_2$ and various organomercury compounds (methylmercury iodide, isopropylmercury bromide, *n*-hexylmercury bromide, phenylmercury bromide, diphenylmercury, *p*-tolylmercury bromide, bis-*p*-tolylmercury) was studied. Mercury compounds exert a dual effect on accumulation of oleic acid hydroperoxide in the temperature range 20–90°C. Below 50°C, the concentration of the hydroperoxides formed in the presence of mercury compounds is lower, and at higher temperatures, higher than in the experiments performed without mercury compounds. Comparison of the concentrations of oleic acid hydroperoxides with those of their transformation products, carbonyl compounds, determined spectrophotometrically, shows that actually organomercury compounds and $HgCl_2$ accelerate peroxide oxidation at all the studied temperatures. Decreased accumulation of peroxides below 50°C is apparently due to the fact that the rate of their reaction with organomercury compounds is higher than the rate of their formation.

Organomercury compounds are highly toxic environmental pollutants. They originate from industrial processes or are formed by biochemical alkylation [1]. Organomercury compounds can accumulate in tissues of living bodies and, owing to lipophilic properties, can readily penetrate through cell membranes. The toxic effect of organomercury compounds was studied in numerous works [1], but its mechanism is still the matter of discussions. According to [2], organomercury compounds suppress cell respiration. At the same time, there are indications that organomercury compounds stimulate an important physiological process, peroxide oxidation of lipids [3].

Peroxide oxidation of lipids has been extensively studied, and several reviews are available [4–6]. This process is a chain reaction which can occur by enzymatic and nonenzymatic pathways. In normal tissues of a living body, the level of peroxide oxidation of lipids is low, and the process is balanced. Disturbance of this balance, e.g., under the action of toxic organomercury compounds, alters the structure of cell membranes, which inevitably leads to various pathologies [7].

It is known that the first stage of oxidation of hydrocarbons RH with molecular oxygen in the presence of an initiator $r^{\cdot}$ (Scheme 1) is a sequence of radical reactions yielding hydroperoxides ROOH, whose concentration in the reaction mixture reaches a maximum. Hydroperoxides further decompose to form alkoxy and hydroxy radicals [8–10].

Scheme 1.

$$r^{\cdot} + RH \longrightarrow R^{\cdot} + rH,$$

$$R^{\cdot} + O_2 \longrightarrow ROO^{\cdot},$$

$$ROO^{\cdot} + RH \longrightarrow ROOH + R^{\cdot},$$

$$ROOH \longrightarrow RO^{\cdot} + OH^{\cdot}.$$

It should be noted that, although a number of general kinetic models have been suggested by now for peroxide oxidation of lipids in biomembranes [10, 11], considerably less attention was given to autooxidation of structural models of lipids such as unsaturated fatty acids, in particular, oleic acid [RH = $CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$ in Scheme 1]. The effect on this process of organomercury compounds as ecotoxicants was not considered previously.

In this work we studied oxidation of oleic acid with atmospheric oxygen in the presence of organomercury compounds of the general formulas $R'HgX$ and R'_2Hg (R' = CH_3, *i*-C_3H_7, *n*-C_6H_{13}, C_6H_5, *p*-$CH_3C_6H_4$; X = Br, I), and also of $HgCl_2$. The reactions were performed for 5 h with continuous air bubbling in a tem-

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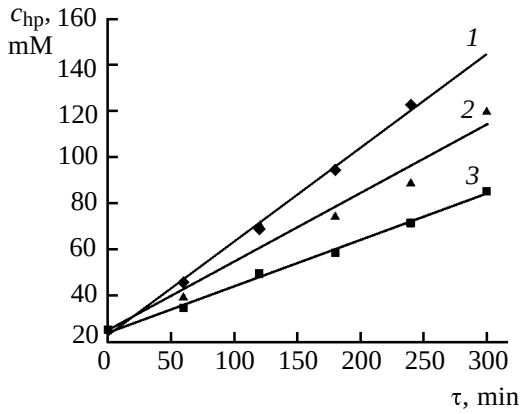

Fig. 1. Variation with time of the concentration of oleic acid hydroperoxides (30°C). Hg compound added (1 mM): (*1*) none, (*2*) CH_3HgI, and (*3*) $HgCl_2$.

perature-controlled vessel at various temperatures. The content of mercury compounds added was 1 mM. Accumulation of oleic acid hydroperoxide was monitored by iodometric titration [12].

We found that organomercury compounds exert a dual effect on accumulation of a total of isomeric oleic acid hydroperoxides ROOH. For example, at 30°C in the presence of organomercury compounds the hydroperoxides are accumulated in smaller amounts than in their absence, i.e., oxidation of oleic acid is seemingly inhibited (Fig. 1). The strongest "inhibiting" effect is observed with $HgCl_2$ and $(C_6H_5)_2Hg$.

At 60°C, the trend becomes reverse: Additions of organomercury compounds noticeably increase the concentration of hydroperoxides (Fig. 2), with this effect being the more pronounced, the higher the concentration of the mercury compound. The largest accelerating effect at 60°C is observed with $(C_6H_5)_2Hg$ and $(p\text{-}CH_3C_6H_4)_2Hg$, and the smallest, with C_6H_5HgBr. Figure 3 shows the ratios C/C_0 for $HgCl_2$ and organomercury compounds at 30 and 60°C (C_0 is the initial concentration of hydroperoxides, and C is their concentration 5 h after the oxidation onset).

Oxidation of oleic acid was also studied spectrophotometrically to monitor accumulation of products formed by decomposition of hydroperoxides. In the presence of $HgCl_2$ and CH_3HgI, an absorption maximum at 224 nm increases, which corresponds to an increase in the concentration of the forming oxidation products, keto acids [13, 14]. These results show that at temperatures below 50°C mercury compounds also accelerate oxidation of oleic acid, but the initially forming hydroperoxides decompose to final oxidation products faster than they are generated.

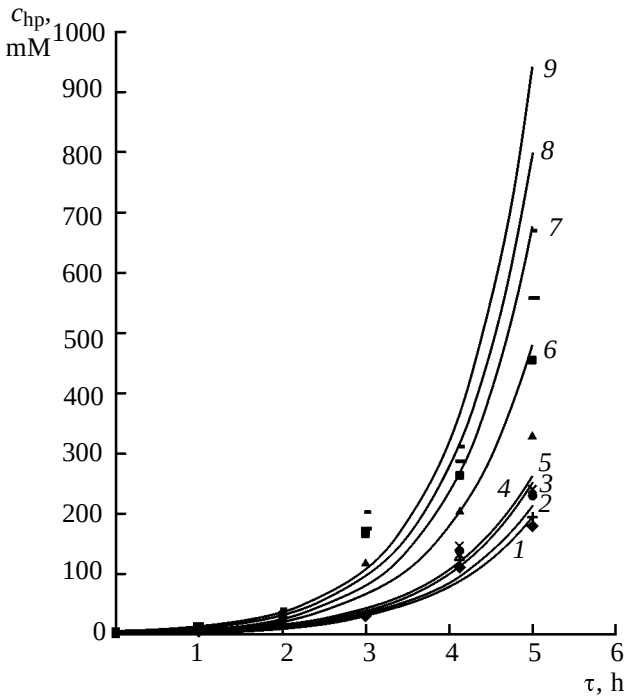

Fig. 2. Accumulation of oleic acid hydroperoxides (60°C) in the presence of mercury compounds (1 mM): (*1*) no addition, (*2*) $p\text{-}CH_3C_6H_4HgBr$, (*3*) C_6H_5HgBr, (*4*) $i\text{-}C_3H_7HgBr$, (*5*) $n\text{-}C_6H_{13}HgBr$, (*6*) CH_3HgI, (*7*) $HgCl_2$, (*8*) $(p\text{-}CH_3C_6H_4)_2Hg$, and (*9*) $(C_6H_5)_2Hg$.

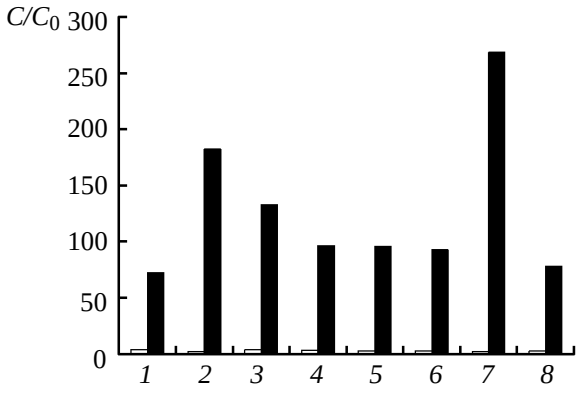

Fig. 3. Ratios C/C_0 obtained at (light bars) 30 and (dark bars) 60°C in the presence of mercury compounds: (*1*) no addition, (*2*) $HgCl_2$, (*3*) CH_3HgI, (*4*) $n\text{-}C_6H_{13}$HgBr, (*5*) $i\text{-}C_3H_7HgBr$, (*6*) C_6H_5HgBr, (*7*) $(C_6H_5)_2Hg$, and (*8*) $p\text{-}CH_3C_6H_4HgBr$.

Figure 4 shows the kinetic curves of keto acid accumulation in the course of oxidation of oleic acid in the presence of $HgCl_2$ and CH_3HgI at 30°C. It is seen that, although addition of mercury compounds decreases at this temperature the content of hydroperoxides (Fig. 1), the content of final oxidation products

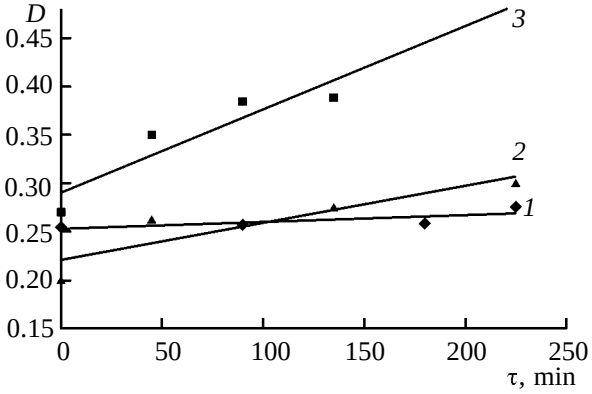

Fig. 4. Oxidation of oleic acid (20°C) in the presence of mercury compounds (1 mM), monitored by the optical density *D* of the reaction mixture. Mercury compound added: (*1*) none, (*2*) CH_3HgI, and (*3*) $HgCl_2$.

and correspondingly the overall oxidation rate increase.

This result can be expained as follows: At low temperatures organomercury compounds react with oleic acid hydroperoxides initially formed in oxidation of oleic acid (Scheme 2).

Scheme 2.

$$R'HgX + ROOH \longrightarrow R'HgOOR + HX,$$

$$R'_2Hg + ROOH \longrightarrow R'HgOOR + R'H,$$

R' = *i*-C_3H_7, *n*-C_6H_{13}, C_6H_5, *p*-$CH_3C_6H_4$; X = Br, I.

Such reactions and mechanisms of further transformations have been well studied [15–17]. The rates of the reactions of R'HgX or R'_2Hg with hydroperoxides ROOH at low temperatures are so high that the concentrations of hydroperoxides in solution become lower than in the experiment without mercury compounds, i.e., the reaction is seemingly inhibited, although actually the additives accelerate oxidation.

At higher temperatures, probably, the kinetic features of the chain reaction of peroxide oxidation change, as indicated by changes in the shapes of the curves of peroxide accumulation or consumption. Below 50°C, these curves are well fitted by a linear function $x = kt + b$. At higher temperatures the dependences become exponential, $x = ae^{ct} + b$, and after taking logarithms linear functions are obtained with the correlation coefficients close to unity. These data suggest that in the bulk of oleic acid acting as solvent with respect to hydroperoxide the reactions are pseudo-first-order. Below are given the initial rates of accumulation of oleic acid hydroperoxides in the absence of additives and in the presence of $HgCl_2$, R'HgX, and R'_2Hg (1 mM) at 60°C.

Additive	–	$HgCl_2$	CH_3HgI
$k \times 10^{-4}$, s^{-1}	2.31 ± 0.1	2.96 ± 0.13	2.78 ± 0.16
Additive	*n*-$C_6H_{13}HgBr$	*i*-C_3H_7HgBr	C_6H_5HgBr
$k \times 10^{-4}$, s^{-1}	2.63 ± 0.12	2.64 ± 0.1	2.67 ± 0.13
Additive	*p*-$CH_3C_6H_4HgBr$	$(C_6H_5)_2Hg$	(*p*-$CH_3C_6H_4)_2Hg$
$k \times 10^{-4}$, s^{-1}	2.69 ± 0.1	3.02 ± 0.13	2.97 ± 0.13

According to the theory of liquid-phase oxidation of hydrocarbons, a change from a linear to an exponential function suggests changes in the character of the chain reaction. The linear function corresponds to the case when the rate of generation of $ROO^{\cdot}$ radicals is comparable with the chain termination rate, whereas accumulation of hydroperoxides by the exponential law corresponds to a chain process with degenerate chain branching. In this case the rate of hydroperoxide formation can increase with time considerably faster than the rate of their decomposition under the action of mercury compounds.

It was shown previously [18] that below 100°C the rate of autooxidation of unsymmetrical mercury compounds R'HgX and of $HgCl_2$ with atmospheric oxygen is extremely low; therefore, the contribution of this process to the overall accumulation of hydroperoxides can be neglected.

Transformations of the arising peroxy radicals $ROO^{\cdot}$, whose concentration in the reaction mixture is comparable with, or higher than the concentration of mercury compounds [8, 10], involve radical substitution at the Hg atom (Scheme 3), with subsequent generation of new free radicals by homolysis of the C–Hg bond [18]. This process accounts for the acceleration of the chain reaction of the substrate oxidation and for the increased amount of the reaction products.

Scheme 3.

$$ROO^{\cdot} + R'HgX \longrightarrow ROOHgX + R'^{\cdot},$$

$$ROO^{\cdot} + R'_2Hg \longrightarrow ROOHgR' + R'^{\cdot},$$

R' = *i*-C_3H_7, *n*-C_6H_{13}, C_6H_5, *p*-$CH_3C_6H_4$; X = Br, I.

To confirm the cleavage of the C–Hg bond, we monitored oxidation of oleic acid in the presence of mercury compounds by IR spectroscopy. The characteristic vibration bands of Hg–C bonds are observed in the range 400–500 cm^{-1}; in particular, in the spectra of crystalline $(C_6H_5)_2Hg$ and C_6H_5HgX these

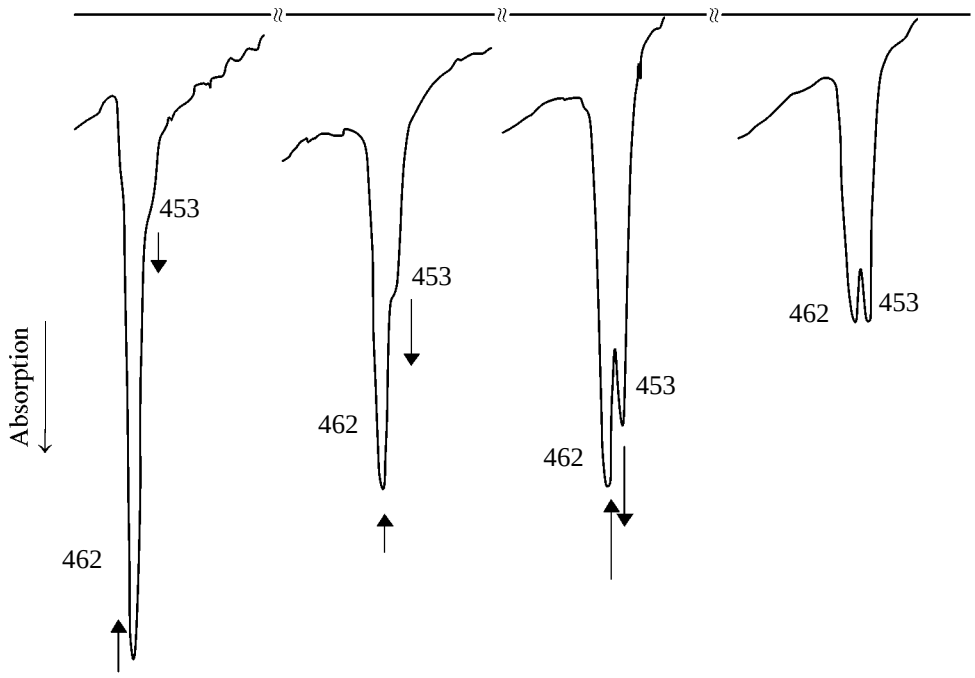

Fig. 5. Variation with time of the IR spectrum of $(C_6H_5)_2Hg$ in oleic acid (frequencies in cm^{-1}) in the presence of atmospheric oxygen. The spectra were recorded at 10-day intervals; concentrations of oleic acid and $(C_6H_5)_2Hg$ 1.53 mM.

bands are located at 456 cm^{-1} [19, 20]. Figure 5 shows the IR spectra of $(C_6H_5)_2Hg$ in oleic acid, monitored at 20°C over the course of 40 days. It is seen that the band at 462 cm^{-1} decreases in intensity, which is accompanied by appearance and growth of a new band at 453 cm^{-1}, corresponding to a species in which one of the C–Hg bonds is cleaved. This pattern is consistent with our assumption (Scheme 2) that diphenylmercury transforms into C_6H_5HgX.

Thus, in the temperature range typical of living bodies organomercury compounds formally do not act as prooxidants, as in their presence the concentration of hydroperoxides decreases. However, monitoring of accumulation of the final oxidation products, keto acids, shows that actually mercury compounds do accelerate peroxide oxidation of oleic acid and hence promote peroxide oxidation of the substrate. An important role in the process is played by free radicals $R'^{\cdot}$ generated by decomposition of organomercury compounds R'HgX and R'_2Hg, and also by hydroxy radicals generated by decomposition of hydroperoxides ROOH. In view of the fact that organomercury compounds can readily penetrate through cell membranes and the local concentration of the toxicant in a cell can considerably exceed its concentration in the surrounding medium, this effect can significantly contribute to the overall toxicity of these compounds.

EXPERIMENTAL

Oleic [(*Z*)-octadecenoic] acid (Sigma) was used without additional purification. The reactions were performed without adding initiators, because these agents could be reactive toward mercury compounds. Oxidation of oleic acid was studied in the temperature range 20–90°C in a temperature-controlled vessel with continuous air supply. The concentration of $HgCl_2$ and organomercury compouynds was 1 mM in all the experiments. The concentrations of hydroperoxides were determined by a standard procedure: iodometric titration with a 0.01 N solution of sodium thiosulfate [12]. The correlation coefficients of the linear dependences were as high as 0.978–0.998. Accumulation of final products of oleic acid oxidation was monitored spectrophotometrically by UV absorption at λ_{max} 224 nm [13, 14]. The electronic absorption spectra were recorded 100 h after the start of the oxidation (20°C) on Varian DMS-100s spectrometers using quartz cells. The organomercury compounds CH_3HgI, *i*-C_3H_7HgBr, *n*-$C_6H_{13}HgBr$, C_6H_5HgBr, *p*-$CH_3C_6H_4HgBr$, $(C_6H_5)_2Hg$, and $(p\text{-}CH_3C_6H_4)_2Hg$ were prepared by standard procedures [21].

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