11-Selenadodecylglyceryl-1-ether in Lipid Autoxidation[1]

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ABSTRACT: The effect of 11-selenadodecylglyceryl-1-ether (11-SeDGE) at concentrations of 5×10^{-4} and 1×10^{-2} M on the autoxidation of sunflower oil with a natural content of 0.06% tocopherols at 100°C and at room temperature in the dark and of pure triacylglycerols of sunflower oil (TGSO) at 100°C was studied. The process was followed by peroxide concentration (peroxide value) determination and by ultraviolet (UV) spectroscopy. It was found that 11-SeDGE acted synergistically with the tocopherols in sunflower oil in a dose-dependent manner to delay oxidation at 100°C. The results from the UV spectra indicated that 11-SeDGE decomposed the initiators of the process, the hydroperoxides, into inactive products. During oxidation of pure TGSO (i.e., depleted of tocopherols) at 100°C, 11-SeDGE retarded the process without a pronounced induction period. At room temperature, 11-SeDGE showed a slight prooxidative effect on sunflower oil oxidation. Taking into account the established prooxidative effect of the two hydroxy groups in a molecule such as 11-SeDGE, it was recommended to study the lipid autoxidation in the presence of selenium compounds that do not contain such prooxidative groups.

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KEY WORDS: Oxidation, 11-selenadodecylglyceryl-1-ether, sunflower oil, synergism, triacylglycerols of sunflower oil, tocopherols.

Selenium (Se) is an essential micronutrient that has important biological activities (1–5). It is considered to strengthen the immune system (6) and to be a protective agent against cancer (7–15),human immunodeficiency virus (14,16), and heart diseases (17–19). Therefore, Se-containing compounds are valuable food constituents (5,19–23) and are included as active components in pharmaceuticals (3,4,24,25) and cosmetics (9,26).

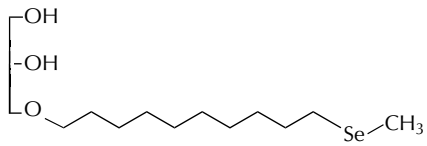
The concentration of selenium and its biological activity are closely related to the reactive oxygen species (27). That is, the higher the concentration of selenium, the greater its biological activity and the lower the concentration of the reactive oxygen species.

Sodium selenate, sodium selenite, selenourea, and selenomethionine display an interesting antioxidant capacity because these derivatives catalyze the disproportionation of the superoxide ion (28). Selenium is a part of the antioxidative enzyme selenoglutathione oxidase, which inactivates free radicals and other oxidants, particularly hydrogen peroxide (29). The biological activity of selenium compounds is related to their antioxidant properties in lipid oxidation in membranes *in vitro* and *in vivo* (2–4,12,18,20,30–36). A synergistic antioxidative effect of selenium with vitamin E has been established (23,37). Vitamin E and selenium show different and complementary antioxidative activities in the living cell (38).

In general, the organoselenium compounds are more biologically active and less toxic than inorganic selenium (39). Already 50 yr ago, Denison and Condit (40) reported on the good antioxidant effectiveness of fatty alcohol selenides, especially didodecyl selenide, in lubricating oils.

Data concerning the effect of selenium compounds on the autoxidation of lipids *in vitro* are sparse. Recently, Vinson *et al*. (19) showed that selenium in the form of ebselen and selenium yeast is a powerful antioxidant *in vitro,* significantly decreasing the lipid peroxides and the oxidation lag time. It was therefore interesting, from a theoretical and practical point of view, to investigate in more detail the effect of organoselenium compounds on lipid oxidation.

In this preliminary study, we used 11-selenadodecylglyceryl-1-ether (11-SeDGE) as a model compound (Scheme 1).



SCHEME 1

Sunflower oil and the triacylglycerols of sunflower oil (TGSO) were the lipid substrates. Sunflower oil, one of the most commonly used oils, contains 60–70% of the essential 9-*cis*,12-*cis*-octadecadienoic (linoleic) acid. The experiments were performed at 100°C and at room temperature at two different concentrations of 11-SeDGE. The process was followed by peroxide concentration [peroxide value (PV)] determination and by ultraviolet (UV) spectroscopy.

MATERIALS AND METHODS

11-SeDGE was synthesized from 11-selenadodecyl-2,3-isopropylideneglycerylether (1.6 g, 4.3 mmol) by refluxing in MeOH (10 mL) and 38% HCl (0.6 mL) for 60 min at 80°C (41). Workup (42) and column chromatography with heptane/acetone (7:3) gave 0.6 g (46%) 11-SeDGE. The structure

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of the compound was verified by mass spectrometry (MS), and ^{1}H and ^{13}C nuclear magnetic resonance (NMR) (41).

A commercial sample of sunflower oil was used. Pure triacylglycerols of sunflower oil (TGSO) were obtained by depleting the sunflower oil of pro- and antioxidants and trace metals by adsorption chromatography (43): 50 g of lipid substrate in 500 mL distilled hexane was passed through a column (2 cm i.d.) filled with 35 g alumina (type 507C, neutral; Fluka AG, Buchs, Switzerland) activated for 4 h at 180°C and collected in the dark under a nitrogen atmosphere. The solvent was removed in a rotary evaporator at 30°C in the dark. The product obtained was stored at –20°C under nitrogen.

The tocopherol content of the sunflower oil was determined by normal-phase high-performance liquid chromatography (HPLC) (44) using a Merck-Hitachi (Darmstadt, Germany) apparatus equipped with a L-6000 pump and a Merck-Hitachi F-1050 fluorescence detector. A Nucleosil SI 50-5, 250 × 4 mm column (Macherey-Nagel, Düren, Germany) was used, and elution was performed with hexane/dioxane (96:4) at a rate of 1 mL/min.

Lipid samples containing 5×10^{-4} and 1×10^{-2} M 11-SeDGE were prepared by adding aliquots of a solution of 11-SeDGE in purified acetone to a weighed lipid sample followed by removal of the solvent with nitrogen.

Oxidation at 100°C (±0.2°C) was carried out by blowing air through the samples (2 g) in the dark at a rate of 100 mL min^{-1}. Oxidation at 22°C (±2°C) was performed in the dark using a 1-mm layer in a petri dish having a diameter of 4 cm. Under the above conditions, the process took place under a kinetic regime, i.e., at sufficiently high oxygen concentration at which the diffusion rate does not influence the oxidation rate. The process was followed by withdrawing samples at measured time intervals, estimating the degree of oxidation by iodometric determination of PV (45), and measuring the content of conjugated dienes by UV spectroscopy. The standard deviations (SD) of the PV determinations (in meq kg^{-1}) were (n = 8): PV = 11.7, SD = 1.1; PV = 33.2, SD = 1.5; PV = 70.7, SD = 5.0; PV = 155.3, SD = 14.0; PV = 405.3, SD = 15.3. The effectiveness of the antioxidants was estimated on the basis of the induction period (IP) determined by the method of the tangents to the two parts of the kinetic curve (46,47). The accumulation of the conjugated dienoic structures formed during the autoxidation of sunflower oil was monitored by UV spectroscopy using a Cecil Series 8000 UV/VIS double-beam scanning spectrophotometer (Cecil Instruments Ltd., Cambridge, United Kingdom). The concentration of the lipid samples in isooctane was 0.2 and 0.05%. Spectra were recorded in the range 200–300 nm. The content of the conjugated dienes was expressed as absorbance at 232 nm [$A_{232\,nm}$ (0.2%)].

RESULTS AND DISCUSSION

The fatty acid composition of TGSO, as determined by gas chromatographic (GC) analysis of methyl esters, was: palmitate, 6%; stearate, 5%; oleate, 25%; linoleate, 64%. The oil contained 0.062% tocopherols (Toc): α-Toc, 88.4%; β-Toc, 3.9%; γ-Toc, 5.1%; δ-Toc, 1.6%; α-tocotrienol (α-Toc-3), 1.0%. The initial PV of the commercial sunflower oil was 7.9 meq kg^{-1}.

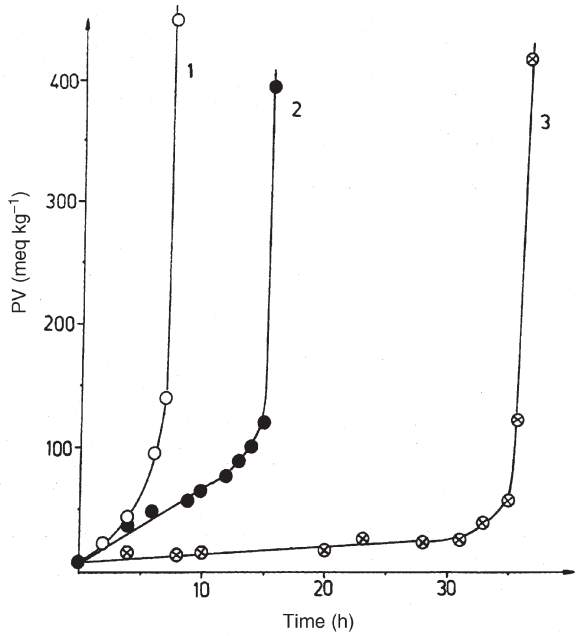

FIG. 1. Kinetic curves of peroxide accumulation during oxidation of sunflower oil at 100°C in the dark in the absence (1) and in the presence of 5×10^{-4} M (2) and 1×10^{-2} M (3) 11-selenadodecylglyceryl-1-ether. PV, peroxide value.

The kinetic curves of peroxide accumulation during oxidation of sunflower oil in the absence and in the presence of 5×10^{-4} and 1×10^{-2} M 11-SeDGE at 100°C are presented in Figure 1. After determining the IP by the method of the tangents to the two parts of the kinetic curves, the following values for the IP were determined: without additive, 6.3 h; in the presence of 5×10^{-4} M 11-SeDGE, 14.8 h; in the presence of 1×10^{-2} M 11-SeDGE, 35.0 h.

The antioxidative effect was estimated on the basis of the stabilization factor **F**:

$$\mathbf{F} = IP_{add}/IP_0 \qquad [1]$$

where IP_{add} is the induction period in the presence of the additive (11-SeDGE), and IP_0 is the induction period of the control lipid sample. The values of **F** for the samples containing 5×10^{-4} and 1×10^{-2} M 11-SeDGE were 2.3 and 5.6, respectively. The data obtained showed that 11-SeDGE increases the oxidative stability of sunflower oil in a concentration-dependent manner.

When a lipid system containing over 30% "methylene-interrupted" fatty acids (e.g., linoleic acid,) is oxidized under a kinetic regime, the only hydroperoxides formed are those of the linoleic acid moiety (48). According to the mechanism of autoxidation (49), linoleic hydroperoxides contain a conjugated double bond structure in their molecules. We monitored the accumulation of conjugated dienes during the oxidation experiments by UV spectroscopy, determining the absorbance at 232 nm, $A_{232\,nm}$. Some of the UV spectra are presented in Figure 2. Figure 3 shows the dependence of $A_{232\,nm}$ on the oxidation time

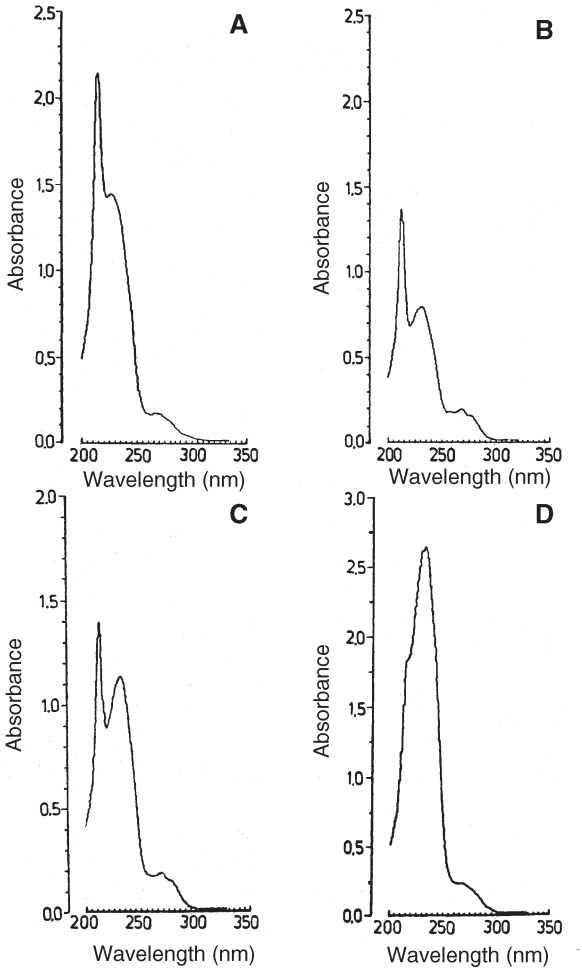

FIG. 2. Ultraviolet spectra of sunflower oil oxidized at 100°C in the dark in the presence of 1×10^{-2} M 11-selenadodecylglyceryl-1-ether. PV, time of oxidation at 100°C (h), and concentration of the oil in isooctane: (A) 7.6 meq/kg, 0 h, 0.2%; (B) 22.0 meq/kg, 28.5 h, 0.05%; (C) 120.0 meq/kg, 36 h, 0.05%; (D) 420.0 meq/kg, 37 h, 0.05%. For abbreviation see Figure 1.

for the control (curve 1) and for the sample with 1×10^{-2} M 11-SeDGE (curve 2). The values for the IP determined from the curves in Figure 3, 6.3 and 35.5 h, respectively, are practically the same, within the experimental error, as those found from the kinetic curves of peroxide accumulation (Fig. 1).

In Figure 4, the correlation between the content of conjugated dienes ($A_{232\,nm}$) and the content of peroxide groups (PV) during the oxidation of sunflower oil in the absence (curve 1) and in the presence of 1×10^{-2} M 11-SeDGE (curve 2) is presented. From the correlations, the parameter $\Delta A_{232\,nm}$ (0.2%)/ΔPV, i.e., how many conjugated dienes correspond to one peroxide unit, was determined. In the absence of 11-SeDGE (curve 1), $\Delta A_{232\,nm}$ (0.2%)/ΔPV is 1.7×10^{-2} kg meq^{-1}. During the induction period of the sample containing 1×10^{-2} M 11-SeDGE (Fig. 4, part A of curve 2), the mean value of $\Delta A_{232\,nm}$ (0.2%)/ΔPV is 5.0×10^{-2} kg meq^{-1} (up to PV = 40 meq kg^{-1}, oxidation time = 33 h). This means that during the IP in the presence of 1×10^{-2} M 11-SeDGE, the concentration of conjugated dienes per peroxide unit is *ca.*

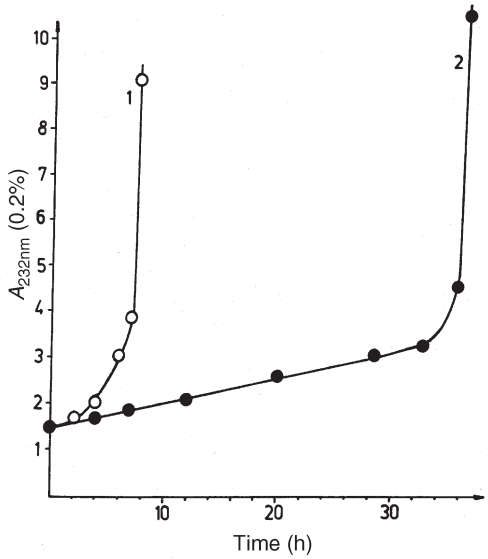

FIG. 3. Kinetic curves of conjugated diene accumulation [$A_{232\,nm}$ (0.2%)] during oxidation of sunflower oil at 100°C in the dark in the absence (1) and in the presence (2) of 1×10^{-2} M 11-selenadodecylglyceryl-1-ether.

three times higher than in its absence. After the end of the IP of the Se-containing sample (Fig. 4, part B of curve 2), the value of $\Delta A_{232\,nm}$ (0.2%)/ΔPV is equal to that for the sunflower oil without 11-SeDGE (Fig. 4, curve 1).

Using 27,000 as a molar absorption coefficient for the conjugated dienes (50), the moles of conjugated dienes (CD) that correspond to one peroxide unit were calculated. For the control sample, the calculated value is 3.15×10^{-4} M CD kg

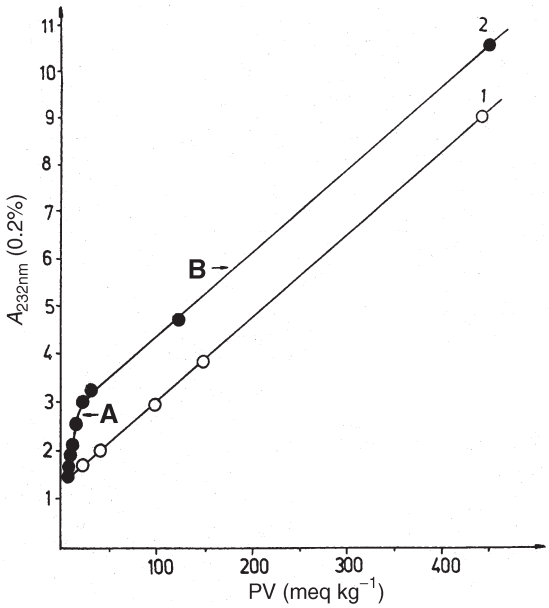

FIG. 4. Correlation between the absorbance of conjugated diene structures [$A_{232\,nm}$ (0.2%)] and the concentration of peroxides, as measured by the PV, during oxidation of sunflower oil at 100°C in the dark in the absence (1) and in the presence (2) of 1×10^{-2} M 11-selenadodecylglyceryl-1-ether. A and B denote the steeply rising and linear portions, respectively of curve 2. For abbreviation see Figure 1.

meq^{-1}, and that for the sample in the presence of 1×10^{-2} M 11-SeDGE is 9.26×10^{-4} M CD kg meq^{-1}.

The precursors of the lipid conjugated diene structures are the linoleic type hydroperoxides, formed by a radical mechanism of oxidation with shifting of one of the double bonds (49,51). The data obtained indicate that, during the IP, 11-SeDGE decomposes the hydroperoxides into inactive products, similarly to some sulfur-containing organic compounds (52,53). Other selenium-containing compounds, e.g., the amino acids selenocysteine or selenomethionine, which are present in trace amounts in natural proteins, also possess hydroperoxide-decomposing activity (29). In contrast to the hydroperoxide groups, the conjugated diene structures are relatively stable at high temperatures (48).

Our results allow the following conclusion: The stabilizing effect of 11-SeDGE originates from its decomposing effect on the lipid hydroperoxides, which are the initiators of the autoxidation process. Hence, 11-SeDGE may be regarded as a synergist for tocopherols, present in sunflower oil, in analogy with the synergism of some sulfur-containing compounds with phenols or amines (54,55). In the body, selenium-containing amino acids help to retain vitamin E (56).

During oxidation of TGSO at 100°C, 11-SeDGE retarded the process without a pronounced IP (Fig. 5). At room temperature and in the dark, 11-SeDGE acted as a prooxidant in sunflower oil (Fig. 6). It was found that 5×10^{-4} and 1×10^{-2} M 11-SeDGE shortened the IP from 45 d (control) to 33 and 29 d, respectively. From the kinetic curves in Figure 6, it can be concluded that 11-SeDGE decomposes the hydroperoxide groups during the IP, because the peroxide concentration during the IP (curves 2 and 3) is lower than that observed with the control (curve 1).

The different effects of 11-SeDGE on the kinetics of sunflower oil oxidation at 100°C and at room temperature could

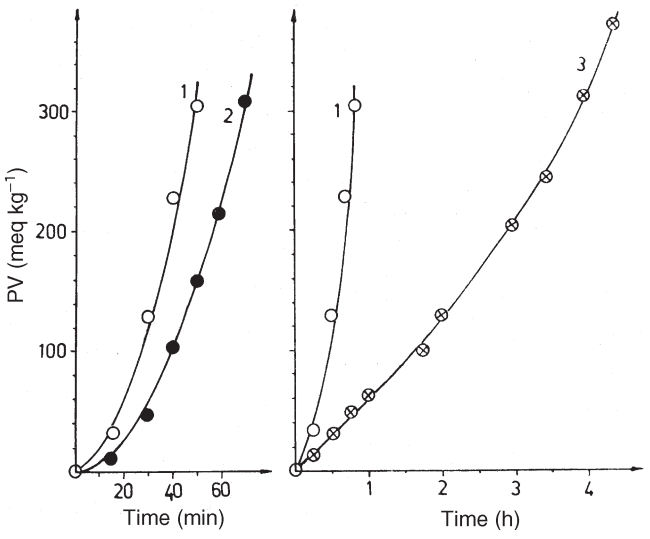

FIG. 5. Kinetic curves of peroxide accumulation during oxidation of triacylglycerols of sunflower oil at 100°C in the dark in the absence (1) and in the presence of 5×10^{-4} M (2) and 1×10^{-2} M (3) 11-selenadodecylglyceryl-1-ether.

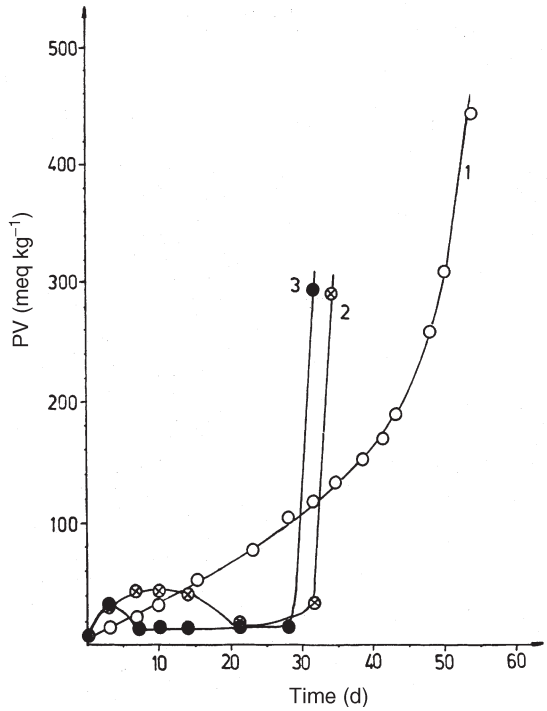

FIG. 6. Kinetic curves of peroxide accumulation during oxidation of sunflower oil at room temperature in the dark in the absence (1) and in the presence of 5×10^{-4} M (2) and 1×10^{-2} M (3) 11-selenadodecylglyceryl-1-ether.

be ascribed to the numerous factors which influence the complex chain radical process of autoxidation. The influence of the different reactions (chain initiation, propagation, termination) on the oxidation rate is temperature dependent (different activation energies) as well.

The presence of free hydroxy groups in 11-SeDGE also may be responsible for its undesirable prooxidative effect at room temperature. As previously verified (57,58), the presence of two hydroxy groups in a molecule, such as in 11-SeDGE, can cause an acceleration of the lipid autoxidation. To exclude the prooxidative effect of the free hydroxy groups in selenamonoglyceryl ethers, the study of selenium compounds without such prooxidative fragments will be performed.

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