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Hemin- and myoglobin-catalyzed reaction of 1-palmitoyl-2-linoleoyl-3-*sn*-phosphatidylcholine 13-hydroperoxide with γ-tocopherol in micelles and liposomes

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ABSTRACT

The secondary process of lipid peroxidation proceeds by the free radical reaction to produce some toxic aldehydes. Since γ-tocopherol (γ-TH), one of the major forms of vitamin E in some vegetable oils, acts as a free radical scavenger, γ-TH may suppress the formation of such aldehydes. This study reports the effect and reaction products of γ-TH on the hemin- or myoglobin-catalyzed decomposition of 1-palmitoyl-2-linoleoyl-3-*sn*-phosphatidylcholine 13-hydroperoxide (PLPC-OOH) in micelles and liposomes. γ-TH and PLPC-OOH in micelles were reacted in the presence of hemin, and the reaction products were characterized as 1-palmitoyl-2-[(8a-dioxy-γ-tocopherone)-12,13-epoxyoctadecenoyl]-3-*sn*-phosphatidylcholines (γT-OO-epoxyPLPC), 1-palmitoyl-2-[(γ-tocopheroxy)-12,13-epoxyoctadecenoyl]-3-*sn*-phosphatidylcholines (γT-epoxyPLPC), and the adducts of γ-TH dimer with PLPC-OOH derived epoxyperoxyl and epoxyalkyl radicals (γTD-OO-epoxyPLPC and γTD-epoxyPLPC). The hemin- and myoglobin-catalyzed decomposition of PLPC-OOH in micelles produced hexanal and 4-hydroxy-2-nonenal as the major aldehydic products. γ-TH suppressed the formation of these aldehydes as the same level as α-TH did, and γ-tocopherylquinone, tocored, γ-TH dimers, and the addition products (γT-OO-epoxyPLPC, γT-epoxyPLPC, γTD-OO-epoxyPLPC, and γTD-epoxyPLPC) were formed during the reaction. In liposomes, hexanal was detected as the major aldehyde and its suppression by γ-TH was less effective than that by α-TH. The results indicate that γ-TH may suppress the formation of aldehydes by trapping the epoxyperoxyl and epoxyalkyl radicals derived from PLPC-OOH although its ability is weak in liposomal systems.

1. Introduction

Lipid hydroperoxides, the primary oxidation products, are decomposed by transition metals and heme compounds to produce a wide range of secondary aldehydic products (Esterbauer et al., 1991; Spiteller et al., 2001), which may exert toxicological effects in biological systems (Blair, 2001; Guéraud et al., 2010; Fritz and Petersen, 2013). Because such aldehydes are formed from lipid hydroperoxides in the course of a radical reaction, some lipid-soluble antioxidants can suppress the formation of these aldehydes (Hayashi et al., 2004). We have reported that α-tocopherol (α-TH), the most active form of vitamin E in biological systems, suppressed the formation of hexanal, one of secondary oxidation products, by trapping free radicals produced by the hemin-catalyzed decomposition of phosphatidylcholine hydroperoxide in micelles and liposomes (Yamauchi et al., 2014).

γ-Tocopherol (γ-TH, Fig. 1) is one of the predominant homologs of vitamin E in dietary sources and acts as a chain-breaking antioxidant in a mechanism similar to α-TH (Eldin and Appelqvist, 1996). γ-TH is structurally different from α-TH only by the absence of a methyl group in the 5-position of the chromanol ring. The unsubstituted 5-position in γ-TH traps lipophilic electrophiles such as reactive nitrogen oxide species and thus counters the oxidative stress (Christen et al., 1997; Jiang, 2014). Devaraj et al. (2008) have reported the effect of γ-TH supplementation alone and in combination with α-TH on biomarker of oxidative stress and inflammation in human subjects with metabolic syndrome, and γ-TH supplementation alone significantly reduced biomarkers of oxidative stress, plasma lipid peroxides as well as malondialdehyde and 4-hydroxy-2-nonenal (HNE), similar to α-TH alone or

Abbreviations: ESI-MS, electrospray ionization mass spectrometry; HNE, 4-hydroxy-2-nonenal; 1H NMR, proton nuclear magnetic resonance spectrometry; HPLC, high-performance liquid chromatography; PDA, photodiode array; PLPC, 1-palmitoyl-2-linoleoyl-3-sn-phosphatidylcholine; PLPC-OOH, 1-palmitoyl-2-[(9Z,11E)-(S)-13-hydroperoxy-9,11-octadecadienoyl]-3-sn-phosphatidylcholine; POPC, 1-palmitoyl-2-oleoyl-3-sn-phosphatidylcholine; γ-TH, γ-tocopherol; γT-epoxyPLPC, 1-palmitoyl-2-[(γ-tocopheroxy)-epoxyoctadecenoyl]-3-sn-phosphatidylcholines; γT-OO-epoxyPLPC, 1-palmitoyl-2-[(8a-dioxy-γ-tocopherone)-epoxyoctadecenoyl]-3-sn-phosphatidylcholines; γTD-epoxyPLPC, adducts of γ-TH dimer with epoxyPLPC radicals; TD-OO-epoxyPLPC, γadducts of γ-TH dimer with epoxyPLPC-peroxyl radicals; γ-TQ, γ-tocopherylquinone; UV, ultraviolet

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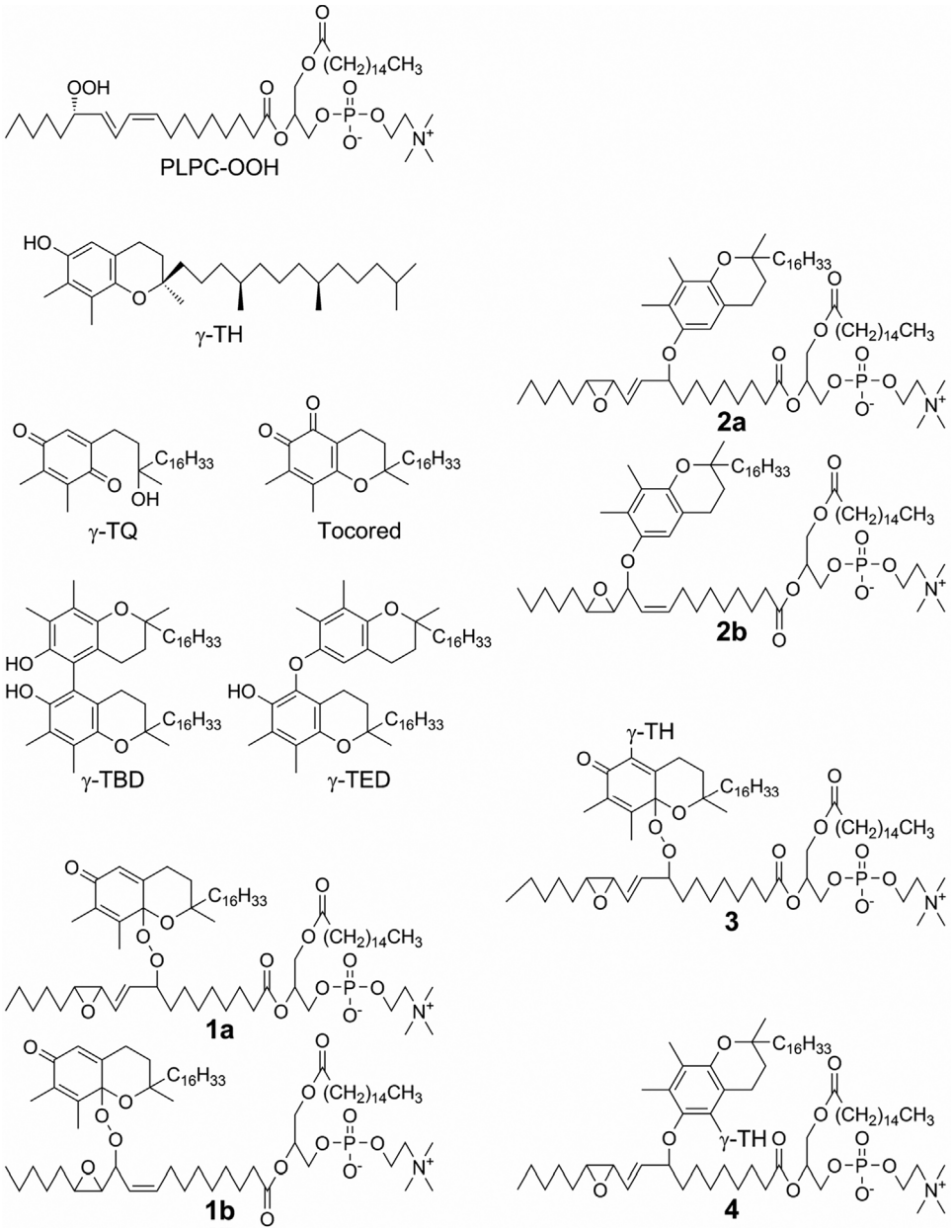

Fig. 1. Structures of compounds referred to in the text. **3** and **4** are shown one of the proposed structures.

the combination. Therefore, γ-TH, along with α-TH, would also be expected to suppress the formation of secondary aldehydic products by trapping lipid-derived free radicals.

In this paper, we have studied the effect of γ-TH on the formation of aldehydic products during the hemin- and myoglobin-catalyzed decomposition of 1-palmitoyl-2-[(9*Z*,11*E*)-(*S*)-13-hydroperoxy-9,11-octadecadienoyl]-3-*sn*-phosphatidylcholine (PLPC-OOH) in micellar and liposomal systems. Hexanal and HNE were measured as the secondary products from PLPC-OOH because these were major aldehydes produced in vivo and in vitro from n-3 polyunsaturated fatty acids during lipid peroxidation. (Schieberle and Grosch, 1981; Umegaki et al., 1999). The reaction products of PLPC-OOH with γ-TH were also investigated to clarify the mechanism of γ-TH action.

2. Materials and methods

2.1. Materials

RRR-γ-TH was purified from mixed isomers of TH (Yamauchi et al., 1990). *RRR*-α-TH was purchased from Sigma-Aldrich Co. (St. Louis, MO). 1-Palmitoyl-2-linoleoyl-3-*sn*-phosphatidylcholine (PLPC) was synthesized as described previously (Yamauchi et al., 1998). PLPC-OOH was prepared by oxidation of PLPC with soybean lipoxygenase as described previously (Yamauchi et al., 2014). 1-Palmitoyl-2-oleoyl-3-*sn*-phosphatidylcholine (POPC) was purchased from NOF Co. (Tokyo, Japan) and used as received. γ-Tocopherylquinone (γ-TQ) was prepared from γ-TH by oxidation with $FeCl_3$ (Kiyose et al., 2001). Tocored (γ-TH-5,6-quinone), atropisomers of γ-TH biphenyl dimer ((*R*)- and (*S*)-5-(γ-tocopherol-5-yl)-γ-tocopherols, γ-TBD), and γ-TH dipherylether dimer (5-(γ-tocopheroxy)-γ-tocopherol, γ-TED) were prepared from γ-TH by reaction with an azo compound (Yamauchi et al., 1990). Hemin (ferriprotoporphyrin chloride) and myoglobin (from equine skeletal muscle) were purchased from Sigma-Aldrich Co. Hemin was dissolved in 20 mM NaOH before use. 2,4-Dinitrophenylhydrazine hydrochloride (DNPH−HCl), hexanal, and heptanal were obtained from Tokyo Chemical Ind. (Tokyo, Japan). 4-Hydroxy-2-nonenal (HNE) was synthesized from 3(*Z*)-nonenal (Gardner et al., 1992). Diethylenetriaminepentaacetic acid (DTPA) and disodium