Sesamin (a compound from sesame oil) Increases Tocopherol Levels in Rats Fed *ad libitum*

Afaf Kamal-Eldin*, Dan Pettersson and Lars-Åke Appelqvist

Department of Food Science, Swedish University of Agricultural Sciences, 750 07 Uppsala, Sweden

ABSTRACT: Six groups of rats were fed diets low, but adequate, in α-tocopherol but high in γ-tocopherol. The six diets differed only in their contents (0, 0.25, 0.5, 1.0, 2.0, and 4.0 g/kg, respectively) of sesamin, a lignan from sesame oil. After four weeks of *ad libitum* feeding, the rats were sacrificed and the concentrations of α- and γ-tocopherols were measured in the plasma, livers, and lungs. Sesamin-feeding increased γ-tocopherol and γ-/α-tocopherol ratios in the plasma ($P < 0.05$), liver ($P < 0.001$), and lungs ($P < 0.001$). The increase was non-significant for α-tocopherol. Thus, sesamin appears to spare γ-tocopherol in rat plasma and tissues, and this effect persists in the presence of α-tocopherol, a known competitor to γ-tocopherol. This suggests that the bioavailability of γ-tocopherol is enhanced in phenol-containing diets as compared with purified diets.

Lipids 30, 499–505 (1995).

Sesame seed (*Sesamum indicum*, Linn., Pedaliaceae) is known for its high nutritional value, and for having high oil (*ca.* 50%) and protein (20–25%) content (1). Sesame oil is characterized by a very high oxidative stability compared with other vegetable oils (2,3). The oil is composed of *ca.* 98% glycerides and 1.5–2% unsaponifiables (4,5). The fatty acid composition of sesame oil is palmitic (7–12%), stearic (3.5–6%), oleic (35–50%), and linoleic acid (35–50%) (4,6,7). Two lignan-type compounds, sesamin and sesamolin, are the major constituents of sesame oil unsaponifiables (5,8). Sesamol (a sesamolin derivative) can be present in sesame seeds and/or oils in very small amounts. Other lignans and sesamol are also present in sesame seeds and/or oils in very small amounts as aglycones, but are present in considerable amounts in the seeds as glucosides (9–14). The structures of all sesame seed lignans are shown in Figure 1, and their systematic names and levels in sesame seeds are presented in Table 1. Crude sesame oil also contains *ca.* 500–700 mg tocopherols per kg, which are about 97% γ-tocopherol (γ-T) (5).

Sesame seed lignans were reported to be responsible for many unique chemical and physiological properties of sesame oil (2,9,15–21). It is of special interest to note that they have antioxidant and antimutagenic properties (9,22). Sesamin has no antioxidant activity in itself, but it is possible that its metabolites can act as antioxidants *in vivo*. Recently, Yamashita *et al.* (23) suggested that certain antioxidants in sesame, other than tocopherols, suppressed senescence in mice. Sesamin also caused a significant increase in γ-T levels in the plasma and liver of rats (24). In their experiment, Yamashita *et al.* (24) studied the effect of addition of sesame seed, sesamin, and sesaminol (a transformation compound from sesamolin in refined sesame oil) to rat diets containing

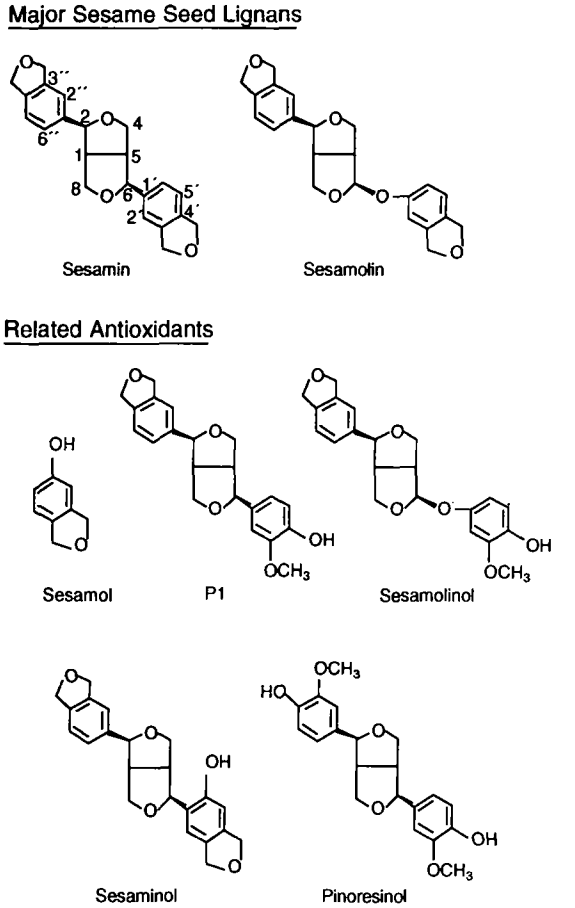

FIG. 1. The chemical structures of sesamin and related compounds in sesame seeds.

*To whom correspondence should be addressed at Dept. of Food Science, Swedish University of Agricultural Sciences, Box 7051, 750 07 Uppsala, Sweden.

Abbreviations: α-T, α-tocopherol; γ-T, γ-tocopherol; GTL, γ-tocopherol levels; HPLC, high-performance liquid chromatography; SL, sesamin levels.

TABLE 1
Trivial and Systematic Names and Levels[a] of Lignans and Lignan Glucosides in Sesame Seeds (*Sesamum indicum*, Linn.)

Trivial names	Systematic names	Weight % in seed	Reference number
Lignans			
Sesamin	2,6-*bis*-(3,4-methylenedioxy phenyl)-*cis*-3,7-dioxabicyclo-[3.3.0]-octane	0.2–0.5	9
Sesamolin	2-(3,4-methylenedioxy phenoxy)-6-(3,4-methylenedioxy phenyl)-*cis*-3,7-dioxabicyclo-[3.3.0]-octane	0.2–0.3	9
Sesamol	3,4-methylenedioxy phenol	0.0004	10
P1	2-(3-methoxy-4-hydroxy phenyl)-6-(3,4-methylenedioxy phenyl)-*cis*-3,7-dioxabicyclo-[3.3.0]-octane	0.002	11
Sesamolinol (P2)	2-(3-methoxy-4-hydroxy phenoxy)-6-(3,4-methylenedioxy phenyl)-*cis*-3,7-dioxabicyclo[3.3.0]-octane	0.006	11
Sesaminol (P3)	2-(3,4-methylenedioxy-6-hydroxy phenyl)-6-(3,4-methylenedioxy phenyl)-*cis*-3,7-dioxabicyclo [3.3.0]-octane	0.002	11
Pinoresinol	2,6-*bis*-(3-methoxy-4-hydroxy phenyl)-*cis*-3,7-dioxabicyclo[3.3.0]-octane	—	12
Lignan glucosides		total *ca.* 1%	12
—	Sesaminol 2′-O-ß-D-glucopyranoside	—	13
—	Sesaminol 2′-O-ß-D-glucopyranosyl(1→2)-ß-D-glucopyranoside	—	13
—	Sesaminol 2′-O-ß-D-glucopyranosyl(1→2)-O-[β-D-glucopyranosyl(1→6)]-ß-D-glucopyranoside	—	13
KP1	Pinoresinol 4′-O-ß-D-glucopyranosyl(1→6)-ß-D-glucopyranoside	—	12
KP2	Pinoresinol 4′-O-ß-D-glucopyranosyl(1→2)-ß-D-glucopyranoside	—	12
KP3	Pinoresinol 4′-O-ß-D-glucopyranosyl(1→2)-O-[ß-D-glucopyranosyl(1→6)]-ß-D-glucopyranoside	—	14

[a]The levels of total lignans and lignan glucosides in sesame seeds can range from 1–1.5%.

practically no α-tocopherol (α-T) but being rich in γ-T. It has been reported that γ-T can be present in plasma at fairly high concentrations in cases of α-T deficiency (25,26). On the other hand, with increased intake, α-T displaces γ-T in serum (27,28) as well as in red blood cells, platelets, and lymphocytes (29).

As mixed diets for humans and animals generally contain both α-T and γ-T as major dietary tocopherols, we considered it relevant to study the effects of dietary sesamin on the retention of γ-T in the rat in the presence of low, but adequate, levels of α-T (30).

MATERIALS AND METHODS

Chemicals and reagents. Sesamin, DL–γ-T and groundnut oil were gifts from Takemoto Oil & Fat Co., Ltd. (Gamagori Aichi, Japan), F. Hoffmann-La Roche (Basel, Switzerland), and from Aarhus Olie (Aarhus, Denmark), respectively. The authentic α- and γ-T used as external standards in high-performance liquid chromatography (HPLC) analyses were purchased from Merck (Darmstadt, Germany). All other chemicals and reagents were of analytical grade and were used without further purification.

Animals, diets, and study design. Thirty-six male, 25-day-old Sprague-Dawley rats (B & K Universal, Sollentuna, Sweden) weighing on average 70 g, were used. The rats were housed individually in wire-bottom cages in a room kept at 25°C and 50% relative humidity. A 12-h light (07:00–19:00)/dark (19:00–07:00) cycle was used. Six groups, of six rats each, were fed the various experimental diets (Table 2). Groundnut oil (containing 13 mg of endogenous α-T and 10 mg of endogenous γ-T per 100 g and fortified with additional γ-T, 40 mg/100 g) was added, at a level of 100 g/kg diet, as a source of energy, essential fatty acids, and vitamin E. Thus, the vitamin E content of the six diets was 13 mg/kg α-T and 50 mg/kg γ-T. Sesamin was the only variable in the diets and was present in diets 1–6 at levels of 0.0, 0.25, 0.50, 1.0, 2.0, and 4.0 g/ kg, respectively. The rats were allowed free access to tap water and were fed experimental diets *ad libitum* for four weeks. Feed was given daily (13:00), and feed wastage was determined at the same time. The rats were weighed every week and the tissues were weighed at sacrifice. This

TABLE 2
Composition of the Basal Experimental Diet[a]

Ingredient	g/kg
Maize starch	570
Casein, vitamin free	200
Groundnut oil[b]	100
Cellulose powder	40
Mineral and trace element premix[c]	40
Sucrose	40
Vitamin premix[d]	10

[a]On dry weight basis, seamin was added to the six diets at levels of 0, 0.25, 0.50, 1.0, 2.0, and 4.0 g/kg diet, respectively.
[b]The groundnut oil had the following fatty acid composition, based on gas chromatographic analysis of the fatty acid methyl esters: 16:0 (12.7%), 18:0 (2.4%), 18:1 (51.3%), 18:2 (31.4%), 20:0 (1.0%), and 20:1 (1.2%). The oil contained (mg/100 g): α-tocopherol (α-T; 13), α-tocotrienol (0.1), ß-tocopherol (0.4), γ-tocopherol (γ-T; 10) and δ-tocopherol (δ-T; 0.6). The oil was supplemented with additional γ-T (40 mg/100 g). Thus, each diet contained 13 and 50 mg/kg of α-T and γ-T, respectively.
[c]The composition of mineral and trace element premix (g/kg) was: Ca, 220; P, 58; Mg, 5; Na, 79; I, 0.065; Se, 0.010; Fe, 2; Co, 0.020; Cu, 0.600; Mn, 2.50; Zn, 3.00.
[d]The composition of the vitamin premix (g/kg) was: vitamin A (retinol), 0.5835; vitamin B_1, 2.57; vitamin B_2, 1.09; vitamin B_6, 1.93; vitamin B_{12}, 0.0028; vitamin C, 0.800; vitamin D_3 (cholecalciferol), 0.0106; pantothenic acid, 3.90; vitamin K_3, 0.430; choline chloride, 188.2; biotin, 0.030; ß-carotene, 0.02; folic acid, 0.27; myo-inositol, 206.4; and nicotinic acid, 8.15.

study was approved by the Ethical Committee for animal experiments of the Uppsala region.

Blood and tissue collections. Rats were deprived of feed for 24 h before sacrifice. Rats were anaesthetized by an intraperitoneal injection of sodium pentobarbital, blood was withdrawn from *vena cava,* and rats were killed by exsanguination. Blood was collected in tubes containing EDTA as anticoagulant, and plasma was isolated following centrifugation (3000 rpm, 4°C, 10 min). The plasma was stored at −20°C until analyzed for tocopherol concentration. The livers and lungs were quickly removed, weighed, immersed in isopropanol (10 mL), and stored at −20°C until analyzed.

Chemical analysis. The tocopherols were extracted from 500 μL portions of the plasma in glass tubes. Ethanol (500 μL) was added to each tube, and the lipids were extracted twice with 2 mL of *n*-hexane after shaking and centrifugation. The lipid extracts were dried over anhydrous sodium sulfate, centrifuged (4000 rpm, 5 min), quantitatively transferred to other tubes, flushed with nitrogen, and sealed and stored at −20°C until analyzed by HPLC within the same or next day. Before HPLC analyses, the hexane extracts were dried under nitrogen and redissolved in 200 μL of hexane.

The livers and lungs were extracted in hexane/isopropanol (3:2, vol/vol) according to Hara and Radin (31) using an Ultra-Turrax homogenizer (Janke and Kunkel GmbH & Co. KG, Breisgau, Germany). Briefly, the livers were homogenized in 100 mL hexane/isopropanol (3:2, vol/vol) and centrifuged at 3000 rpm for 10 min. The lipid extracts were decanted, the tissue was rehomogenized in 50 mL hexane/isopropanol (3:2, vol/vol), and extracts pooled. The extracts were washed twice with aqueous sodium sulfate, and the salt solution was then washed twice with hexane/isopropanol (7:2, vol/vol) (31). The lipid extracts were concentrated under vacuum and transferred to glass tubes containing anhydrous sodium sulfate. The tubes were centrifuged (4000 rpm, 5 min), and the lipid extracts were quantitatively transferred to other tubes. The hexane/isopropanol was evaporated to dryness under nitrogen because α-T has a higher oxidation rate in protic polar solvents. The extracts were then dissolved in hexane, flushed with nitrogen, and sealed and stored at −20°C until analyzed by HPLC within 1–2 d. The solvent was completely evaporated under nitrogen, and the residue was reconstituted in *n*-hexane directly before HPLC analyses.

The tocopherol levels in the plasma and tissues were quantified by HPLC analysis on a Hibar pre-packed LiChrosorb NH_2 column (25 cm × 4 mm i.d., particle size 5 μm; E. Merck). The mobile phase was *n*-heptane/methyl-tertiary butyl ether/tetrahydrofuran/methanol (79:20:1:0.1, by vol) at a flow rate of 1.0 mL/min. The HPLC system consisted of a Merck-Hitachi HPLC L-6200A Intelligent pump, a 20 μL injection loop, and a Merck F-1050 Fluorescence spectrophotometer. The peaks were detected at an excitation wavelength of 295 nm and an emission wavelength of 320 nm, and were recorded using an HP 3396A integrator (Hewlett Packard, Avondale, PA). The tocopherol peaks were identified and quantified against authentic tocopherols used as external standards.

Statistical analysis. Statistical analyses were performed by using the Statistical Analysis System (32). Linear regression analyses of tocopherol concentrations (Y) against sesamin level (X) were done by using the regression procedure (PROC REG) and analysis of variance by using the general linear model with level of sesamin as the only main effect.

RESULTS

The relationships between the sesamin levels in the diets and the α- and γ-T concentrations in the plasma, livers, and lungs of the experimental rats are shown in Figure 2. Positive regression slopes were obtained for both α- and γ-T, showing an increasing effect with increasing sesamin levels in the diets.

For γ-T, the following regression equation was obtained for the plasma: GTL (γ-T level) = 0.270 + 0.214 SL (sesamin level), with a correlation coefficient (r) of 0.60. The intercept (0.270) shows γ-T level (μmole/L plasma) in the control group, and the slope (0.214) shows the rate of increase in γ-T level with increasing sesamin level (SL, g/kg diet) in the experimental groups. The regression equations for γ-T in the liver and lungs were: GTL = 2.913 + 2.072 SL (r = 0.839) and GTL = 1.898 + 2.663 SL (r = 0.86), respectively. The regression analysis procedure showed significant correlations between SL and GTL in plasma ($P < 0.005$), liver ($P < 0.001$), and lungs ($P < 0.001$). On the other hand, the relationships between the sesamin level in the diet (SL) and α-T levels in the plasma, liver, and lungs were not statistically significant (Fig. 2).

The effects of increasing sesamin concentration on the means of α-T, γ-T, and α-T + γ-T levels and on the ratios of γ-T/α-T in the plasma and tissues of experimental rats were assessed by analysis of variance (Table 3). Plasma γ-T concentrations generally increased from 0.06 to 1.07 μmol/L, whereas α-T concentrations varied between 3.06 and 4.79 mmol/L. The concentration of γ-T in the plasma was significantly increased ($P < 0.05$) by sesamin level, whereas the increase in α-T concentration was not statistically significant. The sesamin feeding did not change total body weights nor weights of livers and lungs of experimental rats. In the livers, γ-T increased from 2.12 to 11.03 nmol/g fresh weight ($P < 0.001$) as a result of increasing dietary sesamin. Although α-T concentrations were not significantly changed, they varied between 16.96 and 27.03 nmol/g fresh weight. Similar results were obtained in the lungs, where γ-T concentrations increased from 1.55 to 13.07 nmol/g fresh weight ($P < 0.001$) and α-T concentrations did not change significantly.

DISCUSSION

In this study, the rat diets were rich in γ-T and contained an adequate level of α-T, as judged from the results of Hakkarinen *et al.* (30). The minimum vitamin E requirement for rat survival was reported as 7 mg DL-α-tocopherylacetate per kg

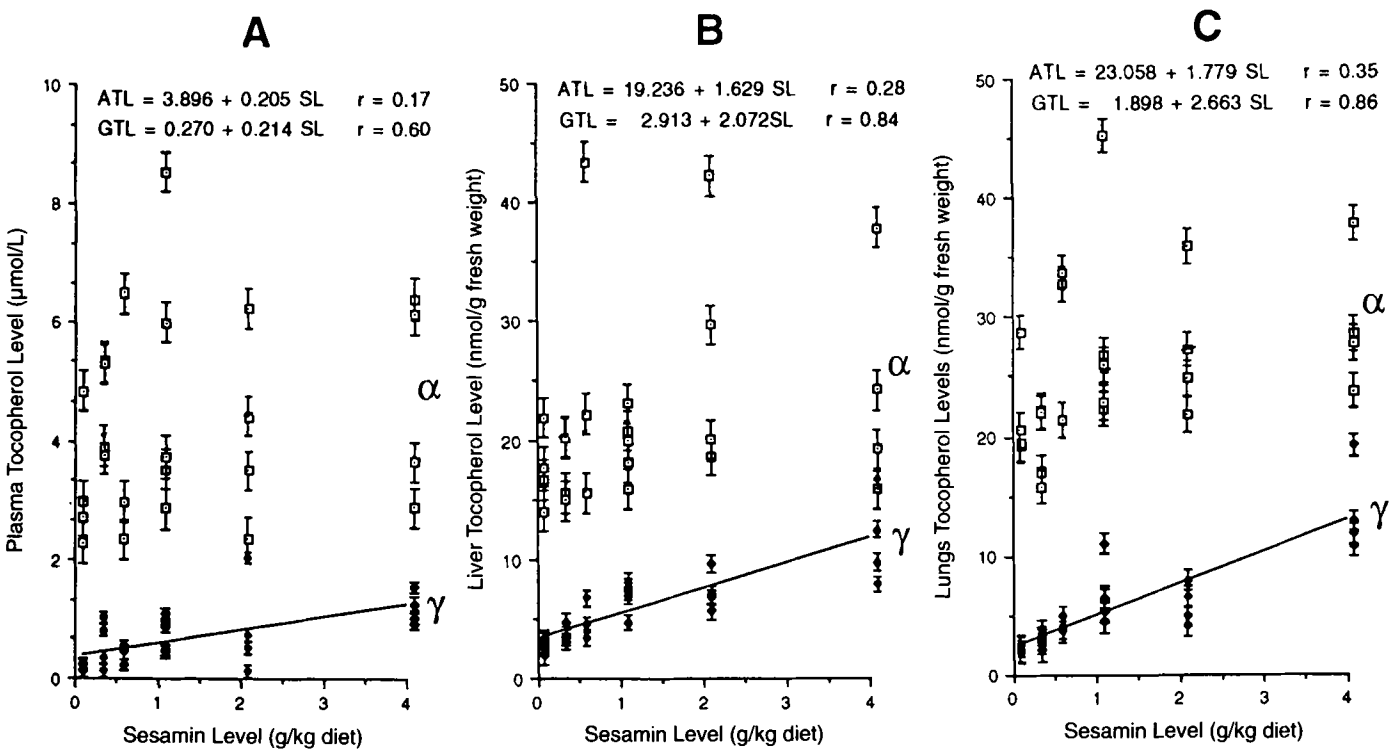

FIG. 2. Linear relationships between α- and γ-tocopherol levels (ATL and GTL, respectively) in rat plasma (A), liver (B), and lungs (C), and sesamin level (SL) in the diet (g/kg). The points show the tocopherol levels for 3–5 rats per sesamin level (group); r denotes the correlation coefficients: the correlations were nonsignificant in the case of α-Tocopherol (α), but significant in the case of γ-tocopherol (γ) (plasma, $P < 0.005$; liver and lungs, $P < 0.001$).

feed when the selenium content of the diet is 6.6 μg/kg and the vitamin E/polyunsaturated fatty acid ratio is 0.45 (30). This experimental approach was introduced to explore if the presence of the adequate α-T levels will mask the reported effect of sesamin on γ-T retention (24). The experiment was designed so that sesamin content was the only differing variable in the experimental diets. Groundnut oil was chosen because of its resemblance to sesame oil in fatty acid composition and for the fact that it contains only α-T and γ-T as major tocopherols (Refs. 4, 6, Table 2).

TABLE 3
Concentrations of α- , γ-, and α + γ-Tocopherols and γ-/α-Tocopherol Ratios in Plasma (μmol/L) and Liver and Lungs (nmol/g wet weight) of Rats Fed a Basal Diet with Increasing Levels of Sesamin[a]

Sesamin level (g/kg diet)	0	0.25	0.50	1.0	2.0	4.0	*P* value for analysis of variance ($P <$)
Number of observations	4	4	3	5	4	4	
Plasma							
α-Tocopherol	3.1 ± 0.56	4.4 ± 0.43	3.8 ± 1.29	4.8 ± 1.04	4.0 ± 0.82	4.6 ± 0.88	N.S.
γ-Tocopherol	0.1 ± 0.03^{b}	0.4 ± 0.21^{b,d}	0.3 ± 0.09^{b,c}	0.6 ± 0.13^{b,d}	0.7 ± 0.41^{c,d}	1.1 ± 0.14^{d}	0.05
α + γ-Tocopherol	3.1 ± 0.54	4.9 ± 0.46	4.1 ± 1.37	5.4 ± 1.11	4.7 ± 1.21	5.7 ± 1.01	N.S.
γ-Tocopherol/α-tocopherol	0.0 ± 0.01^{b}	0.1 ± 0.05^{b,c}	0.1 ± 0.02^{b,c}	0.1 ± 0.03^{c,d}	0.1 ± 0.07^{b,d}	0.2 ± 0.23^{d}	0.05
Liver							
α-Tocopherol	17.0 ± 1.64	17.1 ± 1.45	26.5 ± 8.41	18.9 ± 1.21	27.0 ± 5.45	23.6 ± 4.83	N.S.
γ-Tocopherol	2.1 ± 0.31^{b}	3.0 ± 0.36^{b}	4.2 ± 0.98^{b,c}	6.3 ± 0.60^{c}	6.6 ± 0.85^{c}	11.0 ± 1.90^{d}	0.001
α + γ-Tocopherol	19.1 ± 1.91	20.2 ± 1.42	30.7 ± 9.39	25.2 ± 1.74	33.6 ± 6.26	34.7 ± 6.56	N.S.
γ-Tocopherol/α-tocopherol	0.1 ± 0.01^{b}	0.2 ± 0.03^{b,c}	0.2 ± 0.01^{b,c}	0.3 ± 0.02^{d}	0.3 ± 0.02^{c,d}	0.5 ± 0.05^{e}	0.001
Lungs							
α-Tocopherol	21.3 ± 2.26	18.6 ± 1.67	28.7 ± 3.95	28.1 ± 4.25	26.9 ± 3.03	28.9 ± 2.98	N.S.
γ-Tocopherol	1.5 ± 0.14^{b}	2.3 ± 0.39^{b,c}	3.5 ± 0.40^{b,d}	6.0 ± 1.23^{d}	5.2 ± 0.89^{c,d}	13.1 ± 1.90^{e}	0.001
α + γ-Tocopherol	22.9 ± 2.35^{b}	20.9 ± 1.84^{b}	32.2 ± 4.05^{b,c}	34.1 ± 5.33^{c}	32.1 ± 3.41^{b,c}	42.0 ± 3.70^{c}	0.01
γ-Tocopherol/α-tocopherol	0.1 ± 0.01^{b}	0.1 ± 0.02^{b,c}	0.1 ± 0.02^{b,c}	0.2 ± 0.02^{c}	0.2 ± 0.03^{c}	0.5 ± 0.07^{d}	0.001

[a]Levels of α- and γ-tocopherols measured by HPLC relative to external standards. Values represent means ± SEM (n = 3–5). The composition of the diets is as in Table 2.

^{b,c,d,e}Values within each row not sharing a common superscript letter are statistically different at $P < 0.05$. N.S., not significant.

In the United States, the daily dietary supply of γ-T is approximately twice that of α-T (33,34). Earlier studies showed that the biological activity of γ-T is only about 10–35% of that of α-T (26–28,35,36). Hence, α-T is recognized as the most important natural lipophilic antioxidant in biological systems (36–39). Both isomers (α-T and γ-T) are absorbed to the same extent from the gastrointestinal tract (25,35,40–43), but γ-T is cleared from the tissues at a considerably faster rate than α-T (44,45). Upon feeding equal amounts of the two isomers, both tocopherols were found to increase similarly in the plasma up to 12 h. After 24 h, the level of γ-T decreased drastically, while that of α-T remained almost unchanged (41,43,46). The latter is preferentially bound to the cellular membranes of the liver and to the transporting proteins, while γ-T is excreted through bile without combining with the transporting protein (26,41,43,47). Comparative studies in humans using deuterium-labeled γ-T also showed that there is no discrimination between γ-T and α-T during absorption and secretion in the chylomicrons, but subsequently there is a preferential enrichment of the very low density lipoprotein with α-T (48). All animal studies on relative tocopherol bioavailabilities were conducted using purified diets which contained no antioxidants other than the tocopherols. To date, there is no knowledge about the relative bioavailabilities of the different tocopherols in mixed diets containing other antioxidants, such as plant phenols (49).

Our results are in agreement with previous findings that sesamin-feeding increases γ-T levels in rat plasma and in liver (24). Moreover, we have demonstrated that the effect persists even in the presence of α-T, which is a known competitor to γ-T expression (27–29). In addition, we observed that sesamin induced almost equal increases in the α-T levels in rat plasma, liver, and lungs, although these increases were not statistically significant, perhaps due to the large within-group variation in the levels of this tocol in the plasma and tissues.

The sparing effect of sesamin on vitamin E may explain the observation that some antioxidants, other than tocopherols, in sesame suppressed senescence in mice (23). The resulting increase in total vitamin E bioavailability may also explain some interesting early observations. Tobin (15) reported that daily injection of sesame oil to adrenalectomized female rats increased the number of successful pregnancies, prolonged the survival time of those animals having a successful gestation, and increased their ability to rear young. This effect might have been related to high vitamin E bioavailability as vitamin E is well known to increase fertility in vitamin E-deficient rodents and other animals (50,51). Chou and Marlatt (16) found that sesame oil produced better carotene utilization (a factor of 1.84) than did soybean (1.00) and peanut oils (0.68) when fed to rats. At that time, the effect was surprising as the sesame oil meal contained 11.5 mg tocopherols/kg diet and the soybean oil meal had 27.5 mg /kg. Sesamol was also mentioned to counteract fish oil toxicity to chicks in a similar manner to the antioxidants α-T and x,x′-diphenyl-p-phenyl-enediamine (17).

There is but one report on the absorption of sesamin in rats, where only 0.15% of the fed sesamin was recovered in the lymph during 24 h, suggesting limited absorption (20). Around 15–19% was excreted in the feces in rats fed a purified diet and *ca.* 34% in rats fed a nonpurified diet. The mechanism by which sesamin acts is unknown, but at least two possibilities exist. The mechanism may involve synergistic interaction with γ-T (a regeneration mechanism) in a similar way to other antioxidant synergists, like ascorbic acid. Another possibility is that sesamin may compete with γ-T in its oxidation and/or clearance. Lignans having the methylenedioxyphenyl (1,3-benzodioxole) function are known inhibitors of the mixed function oxidases associated with the endoplasmatic reticulum of the microsomes (52). Many mixed function oxidases are active in the metabolism of lipids, steroids, and in the compounds foreign to the metabolic network (53). Thus, sesamin and related compounds may be regarded as xenobiotic substances by the mixed function oxidases, and their further metabolism may competitively inhibit the activity of these enzymes toward the lipids, sterols, tocopherols, etc.

The sparing of α- and γ-T by sesamin may be of nutritional and physiological significance. A hamburger with a sesame bun, rather common in urban western diets, adds *ca.* 10 mg sesamin to the diet. The metabolism of sesamin in the rat was reported to occur, through the mixed function oxidase enzymes, *via* oxidation of the methylene dioxy function, resulting in a 1,2-diphenol (51), which is expected to have antioxidant properties, at least *in vitro*. Human diets are rich in antioxidant phenols, which may have comparable effects to that of sesamin (49). As sesamin feeding caused a high relative increase in γ-T in rats, we postulate that the bioavailability of γ-T may have been underestimated in the previous studies performed using purified diets (26–28,35,36). The metabolic interaction(s) of γ-T with other food or feed constituents with an antioxidant function needs to be studied further.

ACKNOWLEDGMENTS

We thank Dr. R.V. Cooney (Cancer Research Center, University of Hawaii, Honolulu, HI) for discussions on γ-T and sesame oil during a sabbatical stay (LÅA) at University of Hawaii and for critical reading of the manuscript; Prof. J. Hakkarainen (Department of Clinical Nutrition, this University) for discussions in the preparation for this experiment; Lotta Wall (from this department) for technical assistance; Takemoto Oil & Fat Co., Ltd. (Gamagori Aichi, Japan) and F. Hoffmann-La Roche (Basel, Switzerland) for the sesamin and DL-γ-tocopherol gifts, respectively; and Aarhus Olie (Aarhus, Denmark) for the gift of groundnut oil. The International Science Program in Chemical Sciences (IPICS, Uppsala University) is thanked for extended support to A. Kamal-Eldin.

REFERENCES

1. Weiss, E.A. (1983) *Oilseed Crops*, pp. 292–294, Tropical Agricultural Series, Longman, London.
2. Budowski, P., and Markely, K.S. (1951) The Chemical and Physiological Properties of Sesame Oil, *Chem. Revs. 48*, 125–151.
3. Budowski, P. (1964) Recent Research on Sesamin, Sesamolin and Related Compounds, *J. Am. Oil Chem. Soc. 41*, 280–285.

4. Kamal-Eldin, A., and Appelqvist, L-Å. (1994) Variations in Fatty Acid Composition of the Different Acyl Lipids in Seed Oils from Four *Sesamum* Species, *J. Am. Oil Chem. Soc. 71*, 135–139.
5. Kamal-Eldin, A., and Appelqvist, L-Å. (1994) Variations in the Composition of Sterols, Tocopherols and Lignans in Seed Oils from Four *Sesamum* Species, *J. Am. Oil Chem. Soc. 71*, 149–156.
6. Kamal-Eldin, A., Yousif, G., Iskander, G.M., and Appelqvist, L-Å. (1992) Seed Lipids of *Sesamum Indicum*, L. and Related Wild Species in Sudan. I. Fatty Acids and Triacylglycerols, *Fat Sci. Technol. 94*, 254–259.
7. Spencer, G.F., Herb, S.F., and Gormisky, P.J. (1976) Fatty Acid Composition as a Basis for Identification of Commercial Fats and Oils, *J. Am. Oil Chem. Soc. 53*, 94–96.
8. Kamal-Eldin, A., Appelqvist, L-Å., and Yousif, G. (1994) Lignan Analysis in Seed Oils from Four *Sesamum* Species: Comparison of Different Chromatographic Methods, *J. Am. Oil Chem. Soc. 71*, 141–147.
9. Osawa, T. (1992) Phenolic Antioxidants in Dietary Plants as Antimutagenes, in *Phenolic Compounds in Food and Their Effects on Health. II. Antioxidants and Cancer Prevention* (Hang, M-T., Ho, C-T., and Lee, C.Y., eds.), ACS Symposium Series 507, American Chemical Society, Washington D.C., pp. 135–149.
10. Fukuda, Y., Nagata, Y., Osawa, T., and Namiki, M. (1986) Chemical Aspects of the Antioxidative Activity of Roasted Sesame Seed Oil and the Effects of Using the Oil for Frying, *Agric. Biol. Chem. 50*, 857–862.
11. Fukuda, Y., Osawa, T., Namiki, M., and Ozaki, T. (1985) Studies on Antioxidative Substances in Sesame Seed, *Agric. Biol. Chem. 49*, 301–306.
12. Katsuzaki, H., Kawasumi, M., Kawakishi, S., and Osawa, T. (1992) Structures of Novel Antioxidative Lignan Glucosides Isolated from Sesame Seed, *Biosci. Biotech. Biochem. 56*, 2087–2088.
13. Katsuzaki, H., Kawakishi, S., and Osawa, T. (1994) Sesaminol Glucosides in Sesame Seeds, *Phytochemistry 35*, 773–776.
14. Katsuzaki, H., Kawakishi, S., and Osawa, T. (1993) Structure of Novel Antioxidative Lignan Triglucoside Isolated from Sesame Seed, *Heterocycles 36*, 933–936.
15. Tobin, C.E. (1941) Effects of Adrenolactomy on Pregnancy and Survival of Untreated and Sesame Oil-treated Rats, *Endocrinology 28*, 419–425.
16. Chou, T.C., and Marlatt, A.L. (1953) Factors in the Chinese Diet Affecting Carotene Utilization, *J. Nutr. 51*, 305–315.
17. Ershoff, B.H. (1960) Effects of Diet on Fish Oil Toxicity in the Rat, *J. Nutrition 71*, 45–53.
18. Singhal, P.C., and Joshi, L.D. (1980) Glycemic and Cholesterolemic Role of Ginger and Til, *J. Sci. Res. Plants Med. 4*, 32–34.
19. Sugano, M., Inoue, T., Koba, K., Yoshida, K., Hirose, N., Shinmen, Y., Akimoto, K., and Amachi, T. (1990) Influence of Sesame Lignans on Various Lipid Parameters in Rats, *Agric. Biol. Chem. 54*, 2669–2673.
20. Hirose, N., Inoue, T., Nishihara, K., Sugano, M., Akimoto, K., Shimizu, S., and Yamada, H. (1991) Inhibition of Cholesterol Absorption and Synthesis in Rats by Sesamin, *J. Lipid Res. 32*, 629–638.
21. Shimizu, S., Akimoto, K., Shinmen, Y., Kawashima, H., Sugano, M., and Yamada, H. (1991) Sesamin is a Potent and Specific Inhibitor of Δ^5-Desaturase in Polyunsaturated Fatty Acid Biosynthesis, *Lipids 26*, 512–516.
22. Namiki, M. and Osawa, T. (1986) Antioxidants/Antimutagens in Foods, in *Antiomutagenesis and Anticarcinogenesis Mechanisms* (Shankel, D.M., Hartman, P.E., Kada, T., and Hollaender, A., eds.), Plenum Publishing Corporation, New York, pp. 131–142.
23. Yamashita, K., Kawagoe, Y., Nohara, Y., Namiki, M., Osawa, T., and Kawagishi, S. (1990) Effect of Sesame in the Senescence-Accelerated Mouse, *J. Jpn. Soc. Nutr. Food Sci. 43*, 445–449.
24. Yamashita, K., Nohara, Y., Katayama, K., and Namiki, M. (1992) Sesame Seed Lignans and γ-Tocopherol Act Synergistically to Produce Vitamin E Activity in Rats, *J. Nutr. 122*, 2440–2446.
25. Behrens, W.A., and Madere, R. (1983) Interrelationship and Competition of α- and γ-Tocopherol at the Level of Intestinal Absorption, Plasma Transport and Liver Uptake, *Nutr. Res. 3*, 891–897.
26. Behrens, W.A., and Madere, R. (1987) Mechanism of Absorption, Transport and Tissue Uptake of RRR-α-Tocopherol and d-γ-Tocopherol in the White Rat, *J. Nutr. 117*, 1562–1569.
27. Handelman, G.J., Machlin, L.J., Fitch, K., Weiter, J.J., and Dratz, E.A. (1985) Oral α-Tocopherol Supplements Decrease Plasma γ-Tocopherol Levels in Humans, *J. Nutr. 115*, 807–813.
28. Baker, H., Handelman, G.J., Short, S., Machlin, L.J., Bhagavan, H.N., Dratz, E.A., and Frank, O. (1986) Comparison of Plasma α- and γ-Tocopherol Levels Following Chronic Oral Administration of All-*rac*-α-Tocopheryl Acetate or RRR-α-Tocopheryl Acetate in Normal Adult Male Subjects, *Am. J. Clin. Nutr. 43*, 382–387.
29. Lehmann, J., Rao, D.D., Canary, J.J., and Judd, J.T. (1988) Vitamin E and Relationships Among Tocopherols in Human Plasma, Platelets, Lymphocytes and Red Blood Cells, *Am. J. Clin. Nutr. 47*, 470–474.
30. Hakkarainen, J., Työppönen, J., and Jönsson, L. (1986) Vitamin E Requirement of the Growing Rat During Selenium Deficiency with Special Reference to Selenium Dependent and Selenium Independent Glutathione Peroxidase, *J. Vet. Med. Associ. 33*, 247–258.
31. Hara, A., and Radin, N.S. (1978) Lipid Extraction of Tissues with a Low-Toxicity Solvent, *Anal. Biochem. 90*, 420–426.
32. Statistical Analysis Systems Institute, Inc. (1989) *SAS User's Guide, Version 6, Fourth Edn.*, SAS Institute Inc., Cary, North Carolina.
33. Bieri, J.G., and Evarts, R.P. (1974) Tocopherols and Fatty Acids in American Diets, *J. Am. Diet. Assoc. 62*, 147–151.
34. Lehmann, J., Martin, H.L., Lashley, E.L., Marshall, M.W., and Judd, J.T. (1986) Vitamin E in Foods from High and Low Linoleic Acid, *J. Am. Diet. Assoc. 86*, 1208–1216.
35. Bieri, J.G., and Evarts, R.P. (1974) Vitamin E Activity of γ-Tocopherol in the Rat, Chick and Hamster, *J. Nutr. 104*, 850–857.
36. Dillard, C.J., Gavino, V.C., and Tappel, A.L. (1983) Relative Antioxidant Effectiveness of α-Tocopherol and γ-Tocopherol in Iron-Loaded Rats, *J. Nutr. 113*, 2266–2273.
37. Burton, G.W., Joyce, A., and Ingold, K.U. (1983) Is Vitamin E the Only Lipid-Soluble, Chain-Breaking Antioxidant in Human Blood Plasma and Erythrocyte Membranes? *Arch. Biochem. Biophys. 221*, 281–290.
38. Burton, G.W., and Ingold, K.U. (1986) Vitamin E: Application of the Principles of Physical Organic Chemistry to the Explanation of Its Structure and Function, *Acc. Chem. Res. 19*, 194–201.
39. Diplock, A.T., (1983) The Role of Vitamin E in Biological Membranes, in *Biology of Vitamin E* (Porter, R., and Whelan, J., eds.), pp. 45–55, Pitman, London.
40. Bieri, J.G., and Evarts, R.P. (1974) Gamma-Tocopherol: Metabolism, Biological Activity and Significance in Human Vitamin E Nutrition, *Am. J. Clin. Nutr. 27*, 980–986.
41. Peake, I.R., Windmueller, H.G., and Bieri, J.G. (1972) A Comparison of the Intestinal Absorption, Lymph and Plasma Transport and Tissue Uptake of α- and γ-Tocopherols in the Rat, *Biochem. Biophys. Acta 260*, 679–688.
42. Traber, M.G., Kayden, H.J., Green, J.B., and Green, M.H. (1986) Absorption of Water Miscible Forms of Vitamin E in a

Patient with Cholestasis and in Thoracic Duct-Cannulated Rats, *Am. J. Clin. Nutr. 44*, 914–923.
43. Traber, M.G., and Kayden, H.J. (1989) Preferential Incorporation of α-Tocopherol Versus γ-Tocopherol in Human Lipoproteins, *Am. J. Clin. Nutr. 49*, 517–526.
44. Gloor, U., Wursh, J., Schwieter, U., and Wiss, O. (1966) Resorption, Retention, Verteilung und Stoffwechsel des d,l-α-Tocopherolamines, d,l-N-Methyl-γ-Tocopherolamines und des γ-Tocopherol in Vergleich zum d,l-α-Tocopherol bei der Ratte, *Helv. Chim. Acta 49*, 2303–2312.
45. Peake, I.R., and Bieri, J.G. (1971) Alpha- and Gamma-Tocopherols in the Rat: *in vitro* and *in vivo* Tissue Uptake and Metabolism, *J. Nutr. 101*, 1615–1622.
46. Tran, K., and Chan, A.C. (1992) Comparative Uptake of α- and γ-Tocopherol by Human Endothelial Cells, *Lipids 27*, 38–41.
47. Meydani, M., Cohn, J.S., Macauley, J.B., McNamara, J.R., Blumberg, J.B., and Schaefer, E.J. (1989) Postprandial Changes in the Plasma Concentration of α- and γ-Tocopherols in Human Subjects Fed a Fat-rich Meal Supplemented with Fat-soluble Vitamins, *J. Nutr. 119*, 1252–1258.
48. Traber, M.G., Burton, G.W., Hughes, L., Ingold, K.U., Hidaka, H., Malloy, M., Kane, J., Hyams, J., and Kayden, H.J. (1992) Discrimination Between Forms of Vitamin E by Humans with and Without Genetic Abnormalities of Lipoprotein Metabolism, *J. Lipid Res. 33*, 1171–1182.
49. Shahidi, F., and Wanasundara, J.P.D. (1992) Phenolic Antioxidants, *Crit. Revs. Food Sci. Nutr. 32*, 67–103.
50. Evans, H.M., and Bishop, K.S. (1922) On the Existence of a Hitherto Unrecognized Dietary Factor Essential for Reproduction, *Science 56*, 650–651.
51. Steele, C.E., Jeffery, E.H., and Diplock, A.T. (1974) The Effect of Vitamin E and Synthetic Antioxidants in the Growth *in vitro* of Explanted Rat Embryos, *J. Reprod. Fert. 38*, 115–123.
52. Cassida, J.E. (1970) Mixed Function Oxidase Involvement in the Biochemistry of Insecticidal Synergists, *J. Agric. Food Chem. 18*, 753–772.
53. Mason, H.S., North, J.C., and Vanneste, M. (1965) Microsomal Mixed-Function Oxidations: The Metabolism of Xenobiotics, *Fed. Proc. 24*, 1172–1180.

[Received September 6, 1994, and in revised form February 22, 1995; Revision accepted March 21, 1995]