Vol. 46, No. 6, December 1998 BIOCHEMISTRY *and* MOLECULAR BIOLOGY INTERNATIONAL
Pages 1117–1126

AGE-RELATED CHANGES IN PLASMA AND TISSUE FATTY ACID COMPOSITION IN FISCHER 344 RATS

Marguerite M. Engler,* Mary B. Engler,* Huong Nguyen*

**Laboratory of Cardiovascular Physiology, Department of Physiological Nursing, Box 0610 University of California, San Francisco San Francisco, California 94143-0610*

Received July 17, 1998
Received after revision, August 25, 1998

Summary. Advancing age is associated with increased risk of coronary artery disease. Changes in fatty acid metabolism affect important cellular membrane properties and functions which may contribute to the vascular pathophysiology of aging. This study was designed to investigate the effects of aging on the fatty acid composition of the plasma, liver, aorta, and renal artery in 4-, 15-, and 24-month old Fischer 344 rats, an animal model for aging. With aging, the levels of total polyunsaturated fatty acids (PUFA) increased in the plasma, aorta, and renal artery. The major changes in the liver fatty acid profile were increases in the levels of 18:2n6 and 18:3n3 and a decrease in the levels of 20:3n6 and 20:5n3. The results indicate that significant shifts occur in the levels of n6 and n3 PUFA in the plasma, liver, and vasculature with aging. The alterations in the fatty acid composition may be a pathogenetic mechanism of the vascular changes associated with aging.

Key Words: Aging, lipids, vascular, arachidonic acid, polyunsaturated fatty acids, omega-6, omega-3, liver, renal artery, aorta

INTRODUCTION

Aging is a risk factor for coronary artery disease [1]. It is associated with high vascular resistance and endothelial dysfunction which contributes to the development of atherosclerosis [2-5]. The mechanisms of these age-related vascular changes are not fully understood. However, it is generally agreed that alterations in fatty acid composition may contribute to the vascular pathophysiology in aging [6]. Polyunsaturated fatty acids (PUFA) are integral constituents of cell membrane phospholipids which modulate the cellular properties of signal

Abbreviations: PUFA, polyunsaturated fatty acids; n6, omega-6; n3, omega-3; F344, Fischer 344; VLDL, very-low-density-lipoprotein; LDL, low-density-lipoprotein.

*To whom correspondence should be addressed. Tel: 415-476-0983. Fax: 415-476-8899. E-mail: marguerite_engler_at_s/n-physio @ccmail.ucsf.edu

1039–9712/98/181117–10$05.00/0

transduction, ion transport, enzyme activities, and eicosanoid biosynthesis [7]. Early studies have shown that aging modifies lipid composition and the fluidity of hepatic microsomal and plasma membranes [8-10].

It was first hypothesized that a reduction in the enzyme activity of delta-6-desaturase contributed to the changes in fatty acid composition associated with aging [11]. This enzyme is essential for the conversion of 18:2n6 and 18:3n3 to 20-carbon PUFA of the n6 and n3 series which are the precursors of the vasoactive eicosanoids. Further investigations have documented the effects of aging on the delta-6-desaturase enzymes in rat liver microsomes [12].

Limited research data are available about the effects of aging on the fatty acid metabolism of the vasculature. Therefore, the purpose of this study was to investigate the age-related changes in the fatty acid composition of the aorta and renal artery. It was also of interest to examine the fatty acid composition of the plasma and liver of Fischer 344 rats at different ages (4, 15, and 24 months old).

MATERIALS AND METHODS

Animals. Male Fischer 344 (F344) rats aged 4, 15 and 24 months were obtained from colonies at the National Institute of Aging, Bethesda, Maryland and were maintained on pelleted chow (NIH-31 diet, Teklad, Madison, WI). The mean weights were 305.6 ± 7.6, 424.9 ± 9.4, and 409.4 ± 8.3 gm for 4, 15 and 24 month-old F344 rats, respectively. The animals were acclimated for one week prior to experimentation. Anesthesia was administered with a mixture of oxygen (70%), nitrous oxide (30%) and halothane (5%). Blood was drawn by cardiac puncture in a plastic syringe with sodium citrate (3.8%; 9:1 v/v) as an anticoagulant and plasma was separated by centrifugation at room temperature. The thoracic aorta (1 cm) and the right renal artery (1 cm) were dissected, trimmed of fat and connective tissue, rinsed with cold saline and minced. The liver (1.2 gm) was excised, rinsed with cold saline and homogenized. All experimental procedures were conducted in accordance with the guidelines of the Committee on Animal Research at the University of California, San Francisco.

Lipid extraction and analysis. Total lipids were extracted immediately from the plasma, arteries and liver. The lipid extracts were methylated and the fatty acid composition was determined as previously described [13]. Briefly, fatty acid methyl esters were analyzed using a Hewlett-Packard (HP) model 5890 II gas chromatograph (GC) equipped with a flame ionization detector and a DB-23 fused silica capillary column (0.32 mm ID x 30 M length; J & W Scientific, Folsom, CA). The GC was interfaced with a HP model 3396A integrator and cooled HP model 7673 autosampler. Helium was used as the carrier gas with a flow rate of 2.7 ml/min. The injector and detector temperatures were 250°C and 300°C, respectively. Initial column temperature was 50°C for 2 min followed by temperature programming at a rate of 10°C/min until 180°C and thereafter 5°/min to 240°C. The final temperature was maintained for 15 min. Fatty acids were identified by comparison with standard fatty acid methyl esters (Nu Chek-Prep, Inc., Elysian, MN; Matreya, Pleasant Gap, PA). Fatty acid composition is expressed as percent of total fatty acids.

Statistical analysis. Data were evaluated using analysis of variance (ANOVA), followed by Tukey's test for pairwise comparisons. All data are expressed as mean ± SEM. $P < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

The age-related fatty acid composition of total lipids from the plasma, liver, aorta, and renal artery of F344 rats are shown in Tables 1-4. The major changes observed in the fatty acid composition were significant increases in total PUFA, specifically n6 PUFA, in the plasma, aorta, and renal artery with age. A significant reduction in saturated fatty acids 14:0 and 16:0 as well as the monounsaturated fatty acid 16:1 was also noted in the plasma, aorta, and renal artery of the 15-month and 24-month old F344 rats. The percentage of 20:4n6 FA was significantly increased in the plasma and aorta of 24-month old rats. However, this fatty acid was not detected in the renal artery. The levels of n3 PUFA, 18:3n3 and 22:6n3 FA's, were also decreased in the renal artery of the F344 rats at 24 months.

These findings are the first to document the progression of age-related changes in the fatty acid composition of the vasculature of F334 rats at 4, 15, and 24 months in age. The effects of aging on a large conduit artery and a smaller artery, namely the aorta and the renal artery, were studied. The results also demonstrate that the percentage of total PUFA increases in the vasculature with age. Given the important structural and functional roles of lipids in vascular cell membranes, the alterations in the fatty acid composition may affect membrane fluidity, ion channels, activities of membrane-bound enzymes, and receptors, as well as the biosynthesis of eicosanoids [7]. The changes in PUFA composition may be related to the pathophysiological effects of aging in the vasculature. For example, large arteries become more rigid, which contributes to systolic hypertension with aging [2]. Aging is also associated with endothelial dysfunction in the arterial wall [3-5], which precedes atheromatous plaque formation and clinical evidence of atherosclerosis. Changes in vascular reactivity are also linked to aging. We recently reported that aging increased aortic contractility to norepinephrine and decreased relaxation to acetylcholine in 15- and 24-month-old F334 rats [14]. Acetylcholine evokes endothelium-dependent relaxation, and the previous study provides further evidence of endothelial dysfunction in aging. Moreover, histopathologic examination of the aortas revealed increased media and adventitia thickness in the vessel wall [14]. The data are an exemplar of the vascular pathology associated with aging.

Table 1.
Effect of Aging on the Fatty Acid Composition of Total Lipids* from Plasma of Fischer 344 Rats

Fatty acid	Age (months)		
	4	15	24
13:0	0.3 ± 0.1	0.3 ± 0.0	1.0 ± 0.1[a,b]
14:0	0.7 ± 0.1	0.5 ± 0.1	0.3 ± 0.0[a]
14:1	0.1 ± 0.0	—	—
15:0	0.3 ± 0.0	0.3 ± 0.0	0.2 ± 0.0[a,b]
15:1	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0
16:0	21.2 ± 0.7	20.1 ± 0.4	16.6 ± 0.3[a,b]
16:1	2.3 ± 0.4	1.2 ± 0.2[a]	1.0 ± 0.2[a]
17:0	0.4 ± 0.0	0.3 ± 0.0	0.3 ± 0.0
17:1	0.2 ± 0.0	0.2 ± 0.0	0.1 ± 0.0
18:0	10.0 ± 0.4	9.3 ± 0.5	10.6 ± 0.4
18:1n9	11.9 ± 0.8	12.1 ± 0.6	11.0 ± 0.7
18:1trans	1.5 ± 0.1	1.5 ± 0.1	1.3 ± 0.1
18:2n6	17.6 ± 0.7	19.9 ± 0.5[a,c]	16.0 ± 0.7
18:3n6	0.2 ± 0.0	0.2 ± 0.0	0.4 ± 0.0[a,b]
18:3n3	0.7 ± 0.1	0.6 ± 0.1	0.3 ± 0.0[a,b]
20:0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0
20:1	0.3 ± 0.1	0.2 ± 0.1	0.2 ± 0.0
20:2	0.4 ± 0.0	0.4 ± 0.0	0.3 ± 0.0
20:3n6	0.5 ± 0.0	0.4 ± 0.0	0.4 ± 0.0
20:4n6	10.5 ± 0.7	12.9 ± 0.8	17.8 ± 0.7[a,b]
20:3n3	0.1 ± 0.0	0.1 ± 0.0	—
20:5n3	1.7 ± 0.2	1.2 ± 0.1	0.9 ± 0.1[a,b]
22:0	0.3 ± 0.1	0.2 ± 0.0	0.2 ± 0.0
22:1	0.2 ± 0.1	0.2 ± 0.0	0.1 ± 0.0
22:2n6	0.1 ± 0.0	0.1 ± 0.0	—
22:3n3	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0
22:4n6	0.5 ± 0.1	0.7 ± 0.1	0.6 ± 0.0
24:0	1.6 ± 0.2	1.6 ± 0.1	1.2 ± 0.0
22:6n3	3.9 ± 0.4	4.0 ± 0.2	5.0 ± 0.3
24:1	0.3 ± 0.1	0.3 ± 0.0	0.5 ± 0.1
Σn3	6.5 ± 0.6	6.0 ± 0.2	6.3 ± 0.3
Σn6	29.5 ± 1.2	34.1 ± 1.0[a]	35.0 ± 0.7[a]
Σn6/Σn3	4.8 ± 0.4	5.8 ± 0.4	5.6 ± 0.2
20:4n6/18:2n6	0.6 ± 0.0	0.6 ± 0.1	1.1 ± 0.1[a,b]
20:5n3/18:3n3	2.8 ± 0.5	2.1 ± 0.1	3.2 ± 0.3
Total SAT	35.2 ± 1.1	33.1 ± 0.9	30.8 ± 0.5[a]
Total UNSAT	52.6 ± 1.1	55.8 ± 0.5[a]	55.3 ± 0.6[a]
SAT/UNSAT	0.67	0.59	0.56[a]
Total PUFA	36.0 ± 1.7	40.2 ± 0.9	41.3 ± 0.9[a]

* Values given are % of total fatty acids, 11-13% of total fatty acids could not be identified, n = 7-10. Fatty acids are designated by the number of carbon atoms followed by the number of double bonds. The number of carbon atoms from the last double bond to the methyl end of the molecule is given by nx. All values represent mean ± SEM. SAT represents saturated fatty acids; UNSAT, unsaturated fatty acids; PUFA, polyunsaturated fatty acids; — , not detected. [a]Significantly different than 4 months; [b]15 months; [c]24 months ($p < 0.05$).

Table 2.
Effect of Aging on the Fatty Acid Composition of Total Lipids* from Liver of Fischer 344 Rats

Fatty acid	Age (months)		
	4	15	24
13:0	0.1 ± 0.0	0.1 ± 0.0	0.2 ± 0.0
14:0	0.4 ± 0.1	0.4 ± 0.1	0.3 ± 0.0
14:1	—	—	—
15:0	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0
15:1	—	—	—
16:0	20.4 ± 0.9	21.0 ± 0.6	19.9 ± 0.5
16:1	1.8 ± 0.4	1.1 ± 0.3	0.8 ± 0.2
17:0	0 .5 ± 0.0	0.4 ± 0.0	0.5 ± 0.0
17:1	0.1 ± 0.0	—	—
18:0	17.2 ± 0.5	13.5 ± 0.5[a,c]	18.0 ± 1.2
18:1n9	7.8 ± 0.5	9.7 ± 0.4	9.6 ± 0.7
18:1trans	2.4 ± 0.1	2.4 ± 0.1	2.2 ± 0.1
18:2n6	14.0 ± 0.8	18.2 ± 0.9[a,c]	14.1 ± 0.9
18:3n6	0.2 ± 0.0	0.2 ± 0.0	0.3 ± 0.0[a]
18:3n3	0.3 ± 0.0	0.4 ± 0.0 [a,c]	0.2 ± 0.0
20:0	0.1 ± 0.0	0.1 ± 0.0	—
20:1	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0
20:2	0.4 ± 0.0	0.4 ± 0.0	0.3 ± 0.0
20:3n6	0.9 ± 0.0	0.6 ± 0.0[a]	0.5 ± 0.0[a]
20:4n6	16.0 ± 0.7	14.3 ± 0.6	15.7 ± 0.4
20:3n3	0.1 ± 0.0	0.1 ± 0.0	—
20:5n3	1.6 ± 0.1	0.8 ± 0.0[a]	0.6 ± 0.1[a]
22:0	0.2 ± 0.0	0.3 ± 0.0	0.3 ± 0.0
22:1	—	—	—
22:2n6	0.2 ± 0.0	0.1 ± 0.0	—
22:3n3	0.2 ± 0.0	0.2 ± 0.0	0.3 ± 0.0
22:4n6	0.3 ± 0.0	0.5 ± 0.0[a]	0.5 ± 0.0[a]
24:0	0.4 ± 0.0	0.4 ± 0.0	0.4 ± 0.0
22:6n3	8.2 ± 0.2	7.8 ± 0.3[c]	8.9 ± 0.3
24:1	—	—	—
Σn3	10.3 ± 0.2	9.3 ± 0.3[a]	10.0 ± 0.3
Σn6	31.3 ± 1.3	33.8 ± 1.2 [a]	31.1 ± 0.7
Σn6/Σn3	3.0 ± 0.1	3.7 ± 0.2	3.1 ± 0.1
20:4n6/18:2n6	1.2 ± 0.0	0.8 ± 0.0[a,c]	1.2 ± 0.1
20:5n3/18:3n3	8.0 ± 1.8	2.2 ± 0.2[a]	2.7 ± 0.4[a]
Total SAT	39.9 ± 0.8	36.8 ± 0.6	40.0 ± 1.3
Total UNSAT	53.7 ± 0.7	56.7 ± 0.6	53.9 ± 1.2
SAT/UNSAT	0.74	0.65	0.75
Total PUFA	41.6 ± 1.4	43.1 ± 1.3	41.1 ± 0.8

* Values given are % of total fatty acids, 6-7% could not be identified, n = 7-10. All values represent mean ± SEM. Details are as in Table 1. [a]Significantly different than 4 months; [b]15 months; [c]24 months ($p < 0.05$).

Table 3.
Effect of Aging on the Fatty Acid Composition of Total Lipids* from Aorta of Fischer 344 Rats

Fatty acid	Age (months)		
	4	15	24
13:0	0.2 ± 0.0	0.1 ± 0.0	9.3 ± 1.0[a,b]
14:0	1.5 ± 0.1	0.7 ± 0.1[a]	0.8 ± 0.1[a]
14:1	0.1 ± 0.0	—	0.2 ± 0.0
15:0	0.1 ± 0.0	0.2 ± 0.0	0.2 ± 0.0
15:1	0.3 ± 0.0	0.3 ± 0.1	0.3 ± 0.1
16:0	23.5 ± 0.7	20.4 ± 0.9[a]	17.4 ± 0.8[a,b]
16:1	2.6 ± 0.2	1.3 ± 0.2[a]	0.9 ± 0.2[a]
17:0	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.0
17:1	0.3 ± 0.1	0.5 ± 0.2	0.2 ± 0.1
18:0	10.2 ± 0.5	10.8 ± 0.7	10.1 ± 0.6
18:1n9	16.3 ± 1.0	15.4 ± 1.1	14.8 ± 1.2
18:1trans	2.8 ± 0.1	3.1 ± 0.2	2.9 ± 0.1
18:2n6	13.5 ± 0.9	17.4 ± 1.4	16.2 ± 1.6
18:3n6	0.3 ± 0.1	0.3 ± 0.1	0.1 ± 0.0
18:3n3	0.6 ± 0.1	0.5 ± 0.1	0.4 ± 0.1
20:0	0.5 ± 0.1	0.5 ± 0.2	0.4 ± 0.1
20:1	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0
20:2	0.3 ± 0.0	0.3 ± 0.0	0.4 ± 0.0
20:3n6	0.7 ± 0.1	0.8 ± 0.2	0.6 ± 0.0
20:4n6	5.4 ± 0.5	7.3 ± 0.8	8.2 ± 0.8[a]
20:3n3	—	—	—
20:5n3	0.2 ± 0.0	0.3 ± 0.0	0.3 ± 0.0
22:0	0.6 ± 0.1	0.5 ± 0.2	—
22:1	0.1 ± 0.0	0.2 ± 0.0	0.1 ± 0.0
22:2n6	0.4 ± 0.1	0.3 ± 0.1	0.2 ± 0.1
22:3n3	0.3 ± 0.0	0.2 ± 0.0	0.2 ± 0.0
22:4n6	1.0 ± 0.1	1.2 ± 0.1	1.4 ± 0.1
24:0	0.7 ± 0.2	0.8 ± 0.1	0.8 ± 0.1
22:6n3	1.9 ± 0.1	2.1 ± 0.1	2.6 ± 0.2[a,b]
24:1	0.6 ± 0.1	0.7 ± 0.3	0.5 ± 0.0
Σn3	2.9 ± 0.2	3.1 ± 0.1	3.6 ± 0.2[a]
Σn6	21.1 ± 0.4	27.2 ± 0.7[a]	26.6 ± 0.8[a]
Σn6/Σn3	7.5 ± 0.6	8.9 ± 0.4	7.7 ± 0.6
20:4n6/18:2n6	0.4 ± 0.1	0.5 ± 0.1	0.6 ± 0.1
20:5n3/18:3n3	0.3 ± 0.0	0.8 ± 0.2	0.8 ± 0.2
Total SAT	37.8 ± 0.7	34.5 ± 0.8[a,c]	39.0 ± 0.9
Total UNSAT	47.2 ± 1.4	51.4 ± 1.4	49.5 ± 1.9
SAT/UNSAT	0.80	0.67[a,c]	0.79
Total PUFA	24.0 ± 0.4	30.2 ± 0.7[a]	30.1 ± 0.6[a]

* Values given are % of total fatty acids, 10-14% could not be identified, n = 7-10. All values represent mean ± SEM. Details are as in Table 1. [a]Significantly different than 4 months; [b]15 months; [c]24 months ($p < 0.05$).

Table 4.
Effect of Aging on the Fatty Acid Composition of Total Lipids* from Renal Artery of Fischer 344 Rats

	Age (months)		
Fatty acid	4	15	24
13:0	0.4 ± 0.1	1.0 ± 0.3	3.5 ± 1.0[a]
14:0	2.0 ± 0.1	1.2 ± 0.0[a]	1.0 ± 0.1[a]
14:1	—	—	—
15:0	0.2 ± 0.1	0.3 ± 0.0	0.2 ± 0.0
15:1	0.3 ± 0.0	0.5 ± 0.1[a,c]	0.1 ± 0.0[a]
16:0	26.4 ± 0.9	21.5 ± 0.7[a]	20.7 ± 0.5[a]
16:1	5.0 ± 0.4	2.4 ± 0.2[a]	2.1 ± 0.3[a]
17:0	0.3 ± 0.0	0.3 ± 0.0	0.2 ± 0.0[b]
17:1	0.4 ± 0.1	0.6 ± 0.2	0.2 ± 0.0
18:0	6.5 ± 0.5	5.2 ± 0.3	4.9 ± 0.3[a]
18:1n9	22.6 ± 0.8	21.6 ± 0.5	25.8 ± 0.7[a,b]
18:1trans	3.1 ± 0.1	4.1 ± 0.2[a]	3.8 ± 0.3
18:2n6	18.1 ± 1.1	25.6 ± 1.0[a]	28.0 ± 0.6[a]
18:3n6	0.6 ± 0.1	0.6 ± 0.2	0.2 ± 0.0
18:3n3	1.0 ± 0.1	0.9 ± 0.1	0.7 ± 0.0[a]
20:0	0.6 ± 0.1	0.6 ± 0.1	0.3 ± 0.0
20:1	0.3 ± 0.0	0.3 ± 0.1	0.3 ± 0.0
20:2	—	—	0.3 ± 0.0
20:3n6	2.3 ± 0.3	2.1 ± 0.3	2.1 ± 0.2
20:4n6	—	—	—
20:3n3	—	—	—
20:5n3	0.5 ± 0.1	0.5 ± 0.1	0.1 ± 0.0
22:0	—	—	—
22:1	—	—	—
22:2n6	0.5 ± 0.1	0.4 ± 0.1	0.1 ± 0.0
22:3n3	—	—	—
22:4n6	0.4 ± 0.0	0.3 ± 0.1	0.4 ± 0.0
24:0	0.6 ± 0.0	0.7 ± 0.0	0.6 ± 0.0
22:6n3	1.2 ± 0.1	0.9 ± 0.0	0.9 ± 0.1[a]
24:1	—	—	—
Σn3	2.4 ± 0.1	2.2 ± 0.1	1.7 ± 0.1[a,b]
Σn6	21.3 ± 0.6	29.0 ± 0.5[a]	30.3 ± 0.7[a]
Σn6/Σn3	8.9 ± 0.5	13.6 ± 0.7[a]	18.0 ± 1.0[a,b]
20:4n6/18:2n6	—	—	—
22:6n3/18:3n3	0.6 ± 0.2	0.4 ± 0.1	0.2 ± 0.0
Total SAT	36.4 ± 0.9	30.7 ± 0.4[a]	31.8 ± 0.9[a]
Total UNSAT	55.8 ± 1.2	60.7 ± 1.0[a]	64.0 ± 1.0[a]
SAT/UNSAT	0.65	0.51[a]	0.50[a]
Total PUFA	23.8 ± 0.6	31.2 ± 0.4[a]	32.1 ± 0.7[a]

* Values given are % of total fatty acids, 3-8% could not be identified, n = 7-10. All values represent mean ± SEM. Details are as in Table 1. [a]Significantly different than 4 months; [b]15 months; [c]24 months ($p < 0.05$).

The age-related increases in vascular PUFA composition may also enhance lipid peroxidation. Polyunsaturated fatty acids with multiple double-bond configurations are more susceptible to lipid peroxidation and/or attack by free radicals than saturated or monounsaturated fatty acids [15]. Free radical reactions have been implicated in various diseases such as atherosclerosis, which occur with advancing age. Lipid peroxidation products formed from the PUFA in the vessel wall injure the endothelium [16]. Damage to the endothelial cells or the inner lining of blood vessels is believed to be an initiating event in atherogenesis [17].

Polyunsaturated fatty acids are transported in the circulation by albumin-fatty acid complexes, chylomicrons, very-low-density lipoproteins (VLDL) and low-density lipoproteins (LDL) [18]. The PUFA are then released from the lipid moieties by vascular lipoprotein lipase activity for uptake and incorporation into peripheral tissues. It is of note that plasma and aortic levels of the eicosanoid precursor 20:4n6 was increased with age. Plasma 20:4n6 may arise from hepatic synthesis or release from the adipose tissue. Increased stores of aortic 20:4n6 may be a protective mechanism in aging since 20:4n6 is liberated during cell stimulation by hydrolysis of the membrane phospholipids. It can then be used for subsequent synthesis of vasoactive eicosanoids which modulate vascular tissue. Arachidonic acid may also be metabolized in the aorta since evidence suggests that desaturase and elongase enzymes are present in vascular endothelial cells [19, 20].

PUFA-rich LDL are potential sources of lipid peroxides which can injure and damage the endothelial cells of the vessel wall [16]. LDL which is oxidatively modified through peroxidation of PUFA [21] contributes to the development of atherosclerosis [22]. Results of this study showed that PUFA were increased with age and comprised 30 - 40% of the lipids in the plasma, renal artery, and aorta. This is the same percentage of PUFA that are found in the total fatty acids in the lipids of human serum [23] and atherosclerotic plaques [24]. Therefore, the data indicate that with aging, PUFA are readily available in the arteries and plasma, possibly as circulating free fatty acids or by their incorporation in albumin complexes and lipoproteins.

The primary effects of age at 15 months in the liver were significant increases in the precursors of n6 and n3 PUFA, 18:2n6 and 18:3n3. This was accompanied by significantly decreased levels of 20:3n6, 20:5n3, and 22:6n3. The reduction in 20:3n6 and 20:5n3 persisted in the liver even at 24 months of age. These long chain fatty acids are derived from 18:2n6 and 18:3n3 respectively, through successive delta-6-desaturation and elongation steps [25]. The differences in the fatty acid profile may be attributed to increased hepatic turnover and the

subsequent release of long chain PUFA. Mobilization of these PUFA for eicosanoid biosynthesis may be a compensatory feature of aging. There is also a possibility that these PUFA may be subjected to lipid peroxidation which may reduce their concentration.

In conclusion, the results indicate that the fatty acid composition of the plasma, liver, aorta, and renal artery is significantly altered with aging. PUFA levels are increased in the plasma and vasculature which may enhance the potential for lipid peroxidation. It remains to be determined whether dietary supplementation with a balance of n6 and n3 PUFA can reverse the effects of aging on fatty acid composition in this rat model.

ACKNOWLEDGMENTS

The authors wish to thank Diane Heininger for preparation of the manuscript. This study was supported by Grant NR-02407 from the National Institutes of Health and, in part, by the Research Center for Symptom Management (1 P30 NR-03927), at the University of California, San Francisco. Preliminary data were presented at the 88th Annual Meeting of American Oil Chemists' Society in May 1997, Seattle, Washington.

REFERENCES

1. Gotto, A. M., and Farmer, J. A. (1992) in Heart Disease (Braunwald, E., Ed.) 2nd Edition, pp. 1125-1160, WB Saunders, Philadelphia.
2. Galarza, C. R., Alfie, J., Waisman, G. D., Mayorga, L. M., Camera, L. A., del Rio, M., Vasvari, F., Limansky, R., Farias, J., Tessler, J., and Camera, M. I. (1997) Hypertension **30**, 809-816.
3. Tschudi, M. R., Barton, M., Bersinger, N. A., Moreau, P., Noll, G., Cosentino, F., Malinski, T., and Lüscher, T. F. (1996) J. Clin. Invest. **98**, 899-905.
4. Küng, C. F., and Lüscher, T. F. (1995) Hypertension **25**, 194-200.
5. Zeiher, A. M., Drexler, H., Saurbier, B., and Just, H. (1993) J. Clin. Invest. **92**, 652-662.
6. Horrobin, D. F. (1995) Prostaglandins Leukot. Essent. Fatty Acids **53**, 385-396.
7. Peck, M. D. (1994) J. Nutr. Biochem. **5**, 466-478.
8. Armbrecht, H. J., Birnbaum, L. S., Zenser, T. V., and Davis, B. B. (1982) Exp. Gerontol. **17**, 41-48.
9. Kapitulnik, J., Weil, E., Rabinowitz, R., and Krauss, M. M. (1987) Hepatology **7**, 55-60.
10. Nokubo, M. (1985) J. Gerontol. **40**, 409-414.
11. Horrobin, D. F. (1981) Med. Hypotheses **7**, 1211-1220.
12. Maniongui, C., Blond, J. P., Ulmann, L., Durand, G., Poisson, J. P., and Bezard, J. (1993) Lipids **28**, 291-297.
13. Engler, M. M., Karanian, J. W., and Salem Jr, N. (1991) Alcohol Clin. Exp. Res. **15**, 483-488.
14. Engler, M. B., and Engler, M. M. (1996) Gerontology **42**, 25-35.
15. Halliwell, B., and Chirico, S. (1993) Am. J. Clin. Nutr. **57**, 715S-724S.
16. Dargel, R. (1992) Exp. Toxic Pathol. **44**, 169-181.
17. Lüscher, T. F., and Barton, M. (1997) Clin. Cardiol. **20**, II-3 - II-10.

18. Galli, C., Risé, P., and Marangoni, F. (1995) Prostaglandins Leukot. Essent. Fatty Acids **52**, 103-106.
19. Rosenthal, M. D., and Whitehurst, M. C. (1983) Biochem. Biophys. Acta **750**, 490-496.
20. Rosenthal, M. D. (1987) Biochem. Biophys. Acta **917**, 279-289.
21. Nenseter, M. S., and Drevon, C. A. (1996) Curr. Opin. Lipidol. **7**, 8-13.
22. Steinberg, D., Parthasarathy, S., Carew, T. E., Khoo, J. C., and Witztum, J. L. (1989) N. Engl. J. Med. **320**, 915-924.
23. Patil, V. S., and Magar, N. G. (1960) Biochem. J. **76**, 417-420.
24. Böttcher, C. J., Boelsum-Van Houte, E., Ter Haar Romeny-Wachter, C. C., Woodford, F. P., and Van Gent, C. M. (1960) Lancet **2**, 1162-1166.
25. Galli, C., and Marangoni, F. (1997) Nutrition **13**, 978-985.