Applied nutritional investigation

Fatty acid–binding protein-2 genotype influences lipid and lipoprotein response to eicosapentaenoic acid supplementation in hypertriglyceridemic subjects

Hamideh Pishva Ph.D. a, Soltan-Ali Mahboob Ph.D. b,*, Parvin Mehdipour Ph.D. c, Mohammad Reza Eshraghian Ph.D. d, Javad Mohammadi-Asl Ph.D. e, Saeed Hosseini M.D., Ph.D. f, Farzaneh Karimi B.S. f

a Department of Nutrition and Biochemistry, School of Public Health and Institute of Public Research, Tehran University of Medical Sciences, Tehran, Iran
b Nutrition Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
c Department of Medical Genetics, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
d Department of Epidemiology and Biostatistics, School of Public Health and Institute of Public Research, Tehran University of Medical Sciences, Tehran, Iran
e Department of Genetics, School of Medical Sciences, Ahvaz Jondishapur University of Medical Sciences, Ahvaz, Iran
f Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

Objective: The blood lipid-lowering effects of eicosapentaenoic acid (EPA) on hypertriglyceridemic subjects with different fatty acid–binding protein-2 (FABP2) genotypes have not, to our knowledge, been previously studied.

Methods: Twenty-three FABP2 Ala54 and 23 Thr54 carriers with hypertriglyceridemia (triacylglycerol level > 200 mg/dL) were enrolled in this study. Participants took 2 g of pure EPA daily for 8 wk. Fasting blood lipid and lipoprotein profiles were determined and changes from baseline were measured.

Results: Blood lipids and lipoprotein responses of the FABP2 genotypes differed after EPA supplementation. Changes from baseline for triacylglycerol (19.2% decrease for Ala54 and 60.5% for Thr54, \( P < 0.001 \)), very low-density lipoprotein (20.0% decrease for Ala54 and 60.5% for Thr54, \( P < 0.001 \)), apolipoprotein CIII (22.8% decrease for Ala54 and 36.4% for Thr54, \( P < 0.01 \)), and high-density lipoprotein cholesterol (17.6% increase for Ala54 and 30.7% for Thr54, \( P < 0.01 \)) differed significantly between the two carrier groups. However, changes in total cholesterol, low-density lipoprotein cholesterol, and apolipoprotein B were not significant. EPA supplementation increased plasma EPA in both carrier groups. Although EPA supplementation increased the level of plasma EPA in both carrier groups, this effect was more pronounced in the Thr54 carriers.

Conclusion: Therefore, EPA consumption has more favorable effects on blood lipids of hypertriglyceridemics with Thr54 genotype rather than those with Ala54. The level of plasma EPA increases after EPA supplementation. Because the FABP2 Thr54 polymorphism appears to be prevalent in hypertriglyceridemic subjects, increasing EPA intake in these subjects could be an effective strategy for reducing blood triacylglycerol concentration.

Introduction

Polymorphism in genes involved in fatty acid absorption and metabolism could affect the blood lipid and lipoprotein concentrations. It could also modulate the response to dietary modifications. Fatty acid–binding protein-2 (FABP2) has a low expression in enterocytes of the small intestine and a high affinity for unsaturated and saturated long-chain fatty acids [1–5]. The Thr54 polymorphism of the FABP2 gene is the most common form reported thus far [6,7]. The presence of Thr54 results in an increase in fatty acid uptake from the intestinal lumen [7], and thus Thr54 carriers would be more likely to be prone to the lipidemic effects of dietary fats.

Increasing experimental and clinical evidence suggests that triacylglycerol (TG)-rich lipoproteins play a significant role in the
pathogenesis of atherosclerosis and that the blood TG/high-density lipoprotein cholesterol (HDL-C) ratio is a better predictor of myocardial infarction than total cholesterol (TC)/HDL-C or low-density lipoprotein cholesterol (LDL-C)/HDL-C [8–11]. Consumption of long-chain n-3 fatty acids have been shown to improve blood lipid profile, especially TG levels in dyslipidemic subjects [12]. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are principal long-chain ω-3 fatty acids in the diet [13]. To lower blood TG, an intake of 2–4 g/d of EPA or DHA has been recommended by the American Heart Association [14]. Although DHA and EPA decrease blood TG level, they have different effects on lipoprotein and fatty acid metabolism in human [15]. DHA may elevate concentrations of LDL-C, small very LDL (VLDL), and large LDL particles, and it may increase the mean diameter of the LDL-C particles in fasting plasma [8,16]. Therefore, EPA supplementation may be a better alternative for improving the blood lipid profile in dyslipidemic subjects. Because Thr54 carriers may have a higher absorptive capacity for fatty acids [2–5], we conducted this study to determine the lipid-lowering effects of EPA supplementation in Thr54 and Ala54 carriers.

Materials and methods

Subjects
Participants were selected from hypertriglyceridemic subjects referred from Tehran Central Laboratories to the Endocrinology and Metabolism Research Center (EMRC), Tehran University of Medical Sciences (TUMS), Tehran, Iran. The inclusion criteria were a serum TC level higher than 200 mg/dL (≥2.3 mmol/L) and a fasting blood glucose level lower than 110 mg/dL (≤6.2 mmol/L). Those who received lipid-lowering agents, oral contraceptive pills, diuretics, sex hormones, thyroid medications, ω-3 supplements, had a history of gastrointestinal diseases, and smokers were excluded from the study. In total 170 hypertriglyceridemic subjects were selected and genotyped for Ala54Thr, using a polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP) method. After determination of their FABP2 genotypes, Ala54Thr (gene ID 2169) was genotyped by PCR-RFLP as follows. Exon 2 of the FABP2 gene was amplified by PCR. The PCR amplification of the genomic DNA fragment for FABP2 was performed by the forward primer 5′-ACA CTT GGT ATT ATA GTG ATT AGG 3′- and reverse primer 5′-TAC CCT GAG TTC AGT TTC GTC-3′ [18] (BIONEER, GmbH, Daejeon, Korea). The PCR was performed in a total volume of 20 μL containing 0.5 μL of each primer, 200 ng of DNA, and 10 μL of Taq DNA polymerase 2× master mix (Ampliqon, Copenhagen, Denmark). The amplification protocol consisted of an initial denaturation step at 95 °C for 3 min, followed by 30 cycles of denaturation at 95 °C for 40 s, annealing at 56 °C for 40 s, and extension at 72 °C for 50 s, and a final extension at 72 °C for 5 min. Digestion was performed with 7 μL of the PCR product, incubated with 0.2 μL of Hin6 I (2000 U; Fermentase, Luxamburg, Germany) and 2 μL of 10× restriction Tango buffer (in a total 20-μL reaction) overnight at 37 °C, and then inactivated at 0 °C for 5 min. The digested product was then subjected to electrophoresis on a 4% agarose gel (Boehringer-Mannheim, GmbH, Mannheim, Germany), stained with ethidium bromide (Sinagene, Tehran, Iran), and visualized on a Gel Doc System (U.V.P. Company, Cambidge, UK). A 50-bp ladder (MBI, Fermentase) was used to determine the length of the digested products. The Thr54 allele appeared as a 180-bp fragment after electrophoresis, whereas the Ala54 allele was cleaved by the restriction enzyme and appeared as 99- and 81-bp fragments.

Statistical analyses

The normality of distribution of continuous variables was tested by one-sample Kolmogorov-Smirnov test. To normalize the continuous variables not normally distributed, a log transformation was applied. Differences between serum lipid levels and fatty acid concentrations between the two study groups with different FABP2 genotypes were tested separately by analysis of covariance, and baseline levels of lipids, gender, body mass index, and age were considered covariates. The correlation between TG, VLDL, and ApoCIII and plasma EPA in these subjects with different FABP2 genotypes were measured by Pearson’s correlation coefficients. Test of the difference between the two correlations in Thr54 and Ala54 carriers was also carried out. Because only a few subjects with Thr54/Thr were found among the participants, they were pooled with Ala54/Thr subjects and analyses were carried out on the pooled data. Results are presented as mean ± standard deviation unless otherwise noted. Analyses were performed by SPSS for Windows (SPSS Inc., Chicago, IL, USA). P < 0.05 was considered statistically significant.

Results

The baseline characteristics of participants stratified by gender are listed in Table 1. For comparison of groups with different FABP2 genotypes, the data obtained from Thr54/Thr and Ala54/Thr subjects were combined. EPA supplementation decreased levels of serum lipid and lipoprotein in the two study groups (Table 2). An interaction was observed between FABP2 genotype and the degree of changes in plasma lipids and lipoproteins after EPA consumption. The lipid-lowering effect of EPA supplementation on serum TG, VLDL, and ApoCIII, and its boosting effect on serum HDL-C level were significantly different between the Ala54 and Thr54 carriers (Table 2). Changes from the baseline values for Ala54 and Thr54 carriers are depicted in Figure 1. EPA supplementation increased plasma EPA in Ala54 and Thr54 carriers (Table 3). An interaction was observed between the FABP2 genotype and the change in plasma fatty acid concentrations after EPA supplementation (Table 3). A significant negative correlation was observed between serum lipid profiles (TG, VLDL, ApoCIII) and plasma EPA levels in hypertriglyceridemic subjects after 8 wk of EPA supplementation for Ala54 and Thr54 carriers. The correlation, however, was much stronger in Thr54 than in Ala54 carriers (Table 4).

Although EPA consumption lowered TC and ApoB concentrations in Ala54 and Thr54 carriers, the observed difference between the studied groups was not statistically significant.

Genotyping Ala54Thr (gene ID 2169)

Genomic DNA was extracted from whole blood using the Flexi Gene DNA kit (Qiagen, GmbH, Hilden, Germany). A 180-bp DNA fragment containing the G–A nucleotide substitution in exon 2 (codon 54) of the FABP2 gene (Ala54Thr) was genotyped by PCR-RFLP as follows. Exon 2 of the FABP2 gene was amplified by PCR. The PCR amplification of the genomic DNA fragment for FABP2 was performed by the forward primer 5′-ACA CTT GGT ATT ATA GTG ATT AGG 3′ and reverse primer 5′-TAC CCT GAG TTC AGT TTC GTC-3′ [18] (BIONEER, GmbH, Daejeon, Korea).
Changes in BMI and serum lipids and lipoproteins of hypertriglyceridemic subjects at baseline and after 8-wk eicosapentaenoic acid supplementation in the studied level in Ala54 but not in Thr54 carriers (Table 3).

**Discussion**

Results of the present study clearly show that FABP2 genotypes can influence the lipid-lowering effects of EPA supplementation in hypertriglyceridemic subjects. Although EPA supplementation decreased serum TG, HDL, and ApoCII and increased HDL-C levels in Thr54 and Ala54 carriers, these effects were much pronounced in the Thr54 compared with the Ala54 carriers. Serum levels of TC, LDL-C, and ApoB were decreased in both carriers with no significant differences. FABP2 has a single-ligand binding site with a high affinity for long-chain saturated and unsaturated fatty acids such as EPA [1,7]. It appears that Thr54 carriers could uptake, transport, and metabolize these fatty acids in a more efficient way than Ala54 carriers [2–5]. Consequently, compared with Ala54 carriers, Thr54 carriers may absorb more EPA with equal oral intake and, hence, a greater lipid-lowering effect is observed in the latter group.

Effects of fatty acids on TG and cholesterol metabolism are partly mediated by changes in the expression of lipoprotein lipase and ApoCII. Lipoprotein lipase hydrolyzes the TG component of chylomicron and VLDL particles, which enables the removal of the remaining lipoprotein remnants from circulation by the liver. ApoCIII has an inhibitory effect on lipoprotein lipase activity, and metabolic studies have suggested that high levels of ApoCIII impair the clearance of TG-rich lipoproteins [19]. In the present study, although EPA supplementation decreased serum ApoCIII levels in both studied groups, the decrease in the Thr54 carriers were more significant (Table 3). The TG-lowering effect of EPA has also been attributed to inhibition of hepatic VLDL secretion [20]. Secretion of TG-rich lipoproteins depends on the level of hepatic TG biosynthesis [21]. EPA has been shown to inhibit two key enzymes involved in TG biosynthesis acetyl-coenzyme A:1,2 diacylglycerol acetyl-transferase and phosphatidate hydrolysis. Furthermore, the processes of in vivo TG biosynthesis compete with fatty acid oxidation [21]. EPA may also facilitate hepatic fatty acid oxidation by upregulation of peroxisomal β-oxidation [22]. Furthermore, it

### Table 1
Baseline characteristics of participants

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Genotype</th>
<th>Ala54 (n = 46)</th>
<th>Ala54 (n = 46)</th>
<th>P</th>
<th>Ala54/Thr (n = 19)</th>
<th>Ala54/Thr (n = 19)</th>
<th>P</th>
<th>Ala54 (n = 23)</th>
<th>Ala54/Thr (n = 19)</th>
<th>Ala54/Thr (n = 19)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>%</td>
<td>47.09 ± 10.46</td>
<td>50.46 ± 11.35</td>
<td>&lt;0.05</td>
<td>48.04 ± 1.03</td>
<td>0.342</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>%</td>
<td>27.74 ± 3.45</td>
<td>30.76 ± 6.98</td>
<td>&lt;0.001</td>
<td>28.59 ± 4.8</td>
<td>0.055</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>%</td>
<td>429.48 ± 149.58</td>
<td>367.57 ± 129.60</td>
<td>&lt;0.001</td>
<td>412.03 ± 145.53</td>
<td>0.198</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>%</td>
<td>218.20 ± 39.08</td>
<td>231.24 ± 59.16</td>
<td>&lt;0.001</td>
<td>221.19 ± 45.32</td>
<td>0.386</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>%</td>
<td>117.05 ± 29.09</td>
<td>127.41 ± 43.91</td>
<td>&lt;0.001</td>
<td>119.97 ± 33.73</td>
<td>0.354</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLDL (mg/dL)</td>
<td>%</td>
<td>31.73 ± 7.00</td>
<td>38.77 ± 15.46</td>
<td>&lt;0.001</td>
<td>33.71 ± 11.47</td>
<td>0.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FBG (mg/dL)</td>
<td>%</td>
<td>85.90 ± 29.92</td>
<td>73.55 ± 25.92</td>
<td>&lt;0.001</td>
<td>82.40 ± 29.1</td>
<td>0.198</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ApoB (mg/dL)</td>
<td>%</td>
<td>121.07 ± 24.18</td>
<td>127.81 ± 34.96</td>
<td>&lt;0.001</td>
<td>122.97 ± 27.4</td>
<td>0.458</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ApoCIII (mg/dL)</td>
<td>%</td>
<td>17.08 ± 1.59</td>
<td>15.34 ± 4.38</td>
<td>&lt;0.001</td>
<td>15.69 ± 4.9</td>
<td>0.291</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

***Values indicate differences between post and pre intervention.***

### Table 2
Changes in BMI and serum lipids and lipoproteins of hypertriglyceridemic subjects at baseline and after 8-wk eicosapentaenoic acid supplementation in the studied groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Genotype</th>
<th>Ala54 (n = 23)</th>
<th>Ala54 (n = 23)</th>
<th>P</th>
<th>Ala54/Thr (n = 19)</th>
<th>Ala54/Thr (n = 19)</th>
<th>P</th>
<th>Ala54 (n = 23)</th>
<th>Ala54/Thr (n = 19)</th>
<th>Ala54/Thr (n = 19)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before intervention</td>
<td></td>
<td>27.83 ± 3.14</td>
<td>28.11 ± 3.17</td>
<td>&lt;0.05</td>
<td>29.48 ± 6.17</td>
<td>29.70 ± 6.19</td>
<td>&lt;0.05</td>
<td>0.284 ± 0.45</td>
<td>0.3 ± 0.46</td>
<td>0.648</td>
<td></td>
</tr>
<tr>
<td>After intervention</td>
<td></td>
<td>27.83 ± 3.14</td>
<td>28.11 ± 3.17</td>
<td>&lt;0.05</td>
<td>29.48 ± 6.17</td>
<td>29.70 ± 6.19</td>
<td>&lt;0.05</td>
<td>0.284 ± 0.45</td>
<td>0.3 ± 0.46</td>
<td>0.648</td>
<td></td>
</tr>
<tr>
<td>BML (kg/m²)</td>
<td>%</td>
<td>27.83 ± 3.14</td>
<td>28.11 ± 3.17</td>
<td>&lt;0.05</td>
<td>29.48 ± 6.17</td>
<td>29.70 ± 6.19</td>
<td>&lt;0.05</td>
<td>0.284 ± 0.45</td>
<td>0.3 ± 0.46</td>
<td>0.648</td>
<td></td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>%</td>
<td>218.42 ± 35.39</td>
<td>199.29 ± 33.62</td>
<td>&lt;0.001</td>
<td>225.35 ± 54.10</td>
<td>196.53 ± 50.11</td>
<td>&lt;0.001</td>
<td>19.03 ± 22.10</td>
<td>28.81 ± 26.76</td>
<td>0.702</td>
<td></td>
</tr>
<tr>
<td>TC (mg/dL)</td>
<td>%</td>
<td>123.93 ± 24.93</td>
<td>108.36 ± 25.47</td>
<td>&lt;0.01</td>
<td>116.93 ± 41.07</td>
<td>108.32 ± 28.08</td>
<td>0.121</td>
<td>13.94 ± 17.99</td>
<td>8.60 ± 25.57</td>
<td>0.336</td>
<td></td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>%</td>
<td>37.51 ± 8.21</td>
<td>44.23 ± 10.81</td>
<td>&lt;0.001</td>
<td>39.23 ± 13.04</td>
<td>40.26 ± 10.85</td>
<td>&lt;0.001</td>
<td>6.62 ± 4.61</td>
<td>10.43 ± 6.44</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>VLDL (mg/dL)</td>
<td>%</td>
<td>68.43 ± 22.93</td>
<td>55.20 ± 22.34</td>
<td>&lt;0.001</td>
<td>96.39 ± 28.26</td>
<td>46.63 ± 16.39</td>
<td>&lt;0.001</td>
<td>13.23 ± 6.13</td>
<td>49.75 ± 6.13</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>FGB (mg/dL)</td>
<td>%</td>
<td>102.98 ± 6.91</td>
<td>91.24 ± 7.69</td>
<td>&lt;0.001</td>
<td>101.57 ± 6.71</td>
<td>92.05 ± 7.85</td>
<td>&lt;0.001</td>
<td>9.74 ± 6.68</td>
<td>10.06 ± 6.12</td>
<td>0.523</td>
<td></td>
</tr>
<tr>
<td>ApoB (mg/dL)</td>
<td>%</td>
<td>122.76 ± 21.38</td>
<td>104.24 ± 33.80</td>
<td>&lt;0.01</td>
<td>123.19 ± 32.85</td>
<td>111.41 ± 25.61</td>
<td>&lt;0.01</td>
<td>18.52 ± 28.94</td>
<td>11.78 ± 17.35</td>
<td>0.538</td>
<td></td>
</tr>
<tr>
<td>ApoCIII (mg/dL)</td>
<td>%</td>
<td>14.53 ± 8.21</td>
<td>11.30 ± 3.40</td>
<td>&lt;0.001</td>
<td>16.65 ± 3.19</td>
<td>12.31 ± 3.90</td>
<td>&lt;0.001</td>
<td>3.23 ± 2.28</td>
<td>6.34 ± 3.60</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

*Apob, apoprotein B; ApoC3, apoprotein CIII; BMI, body mass index; FG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triacylglycerol; VLDL, very low-density lipoprotein.*

*Values are expressed ± SDs unless noted otherwise.

† Carriers are expressed as frequency (percentage), and independent t test was carried out between blood parameters and respective sexes.

‡ Significant difference between Ala54 and Ala/Thr + Thr/Thr groups.

§ Paired t test.
may also interact with transcription factors regulating fatty acid oxidation in mitochondria [23–25]. This results in slower formation of TG-rich VLDL particles in those who take EPA.

Consumption of fish oil has been shown to increase level of HDL-C [25–27]. In the present study, EPA supplementation increased serum HDL-C level in both genotypes studied. Similar to what was observed for serum TG, EPA supplementation was more effective in Thr54 carriers. EPA has been shown to decrease cholesteryl ester transfer protein activity [28]. Because cholesteryl ester transfer protein lowers HDL-C by transferring cholesteryl esters to LDL-C and VLDL particles, a decrease in its activity could result in higher HDL-C concentrations.

In a study by Dworatzek et al. [29], consumption of a test meal containing olive oil increased postprandial chylomicron cholesterol in T54 carriers and a non-significant increase was also observed in chylomicron TG of these subjects. Although the lowering effect of ω-3 fatty acids on serum TG concentrations of hypertriglyceridemic subjects has been shown in several supplementation studies [30–33], no consistent results have been obtained regarding TC, LDL-C, and ApoB concentrations.

In conclusion, EPA consumption has greater lipid-lowering effect in hypertriglyceridemic Thr54 carriers. Because the Thr54 polymorphism of FABP2 appears to be more prevalent in hypertriglyceridemic subjects, increasing EPA intake in these subjects could be an effective strategy to reduce their blood TG levels.

Acknowledgments

The authors thank all the subjects who participated in this study, the staff of the Danesh, Kach, Masood, Nour, and EMRC laboratories, and Shariaty Hospital Heart Diseases Center, Tehran. They thank Professor Hamid Reza Sadeghipour-Roodsary and Javad Nasrollahzadeh for their useful comments on their work.
conducting this study. They are also grateful to Dr. Farokh Habibzadeh for his editing of the manuscript. The EPA caps were a kind gift from Minammi Nutrition, Belgium.

References


[8] Kelley DS, Siegel D, Vemuri M, Mackey BE. Docosahexaenoic acid supplemen-
tation improves fasting and postprandial lipid profiles in hyper-


[16] Schoonjans K, Staels B, Auwerx J. Role of the peroxisome proliferator-

[17] Berge RK, Madsen L, Vaaghehs L, Tronstad KJ, Gottlieber M, Rastek A. In con-
trast with docosahexaenoic acid, eicosapentaenoic acid and hypo-
lipidaemic derivatives decrease hepatic synthesis and secretion of tri-

[18] Dagnelie PC, Rietveld T, Swart GR, Sijsters T, Vanden Berg JW. Effect of dietary fish oil on blood levels of free fatty acids, ketone bodies and tri-


[22] Berge RK, Madsen L, Vaaghehs L, Tronstad KJ, Gottlieber M, Rastek A. In con-
trast with docosahexaenoic acid, eicosapentaenoic acid and hypo-
lipidaemic derivatives decrease hepatic synthesis and secretion of tri-

[23] Dagnelie PC, Rietveld T, Swart GR, Sijsters T, Vanden Berg JW. Effect of dietary fish oil on blood levels of free fatty acids, ketone bodies and tri-