Effect of α-linolenic acid in the human diet on linoleic acid metabolism and prostaglandin biosynthesis

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Abstract The effect of dietary α-linolenic acid intake on linoleic acid metabolism and prostaglandin (PG) biosynthesis was investigated in two groups of six healthy females (25–32 yr). They were given isocaloric formula diets (FD) containing linoleic acid at a constant intake (4% of calories), with different amounts of α-linolenic acid: 0% (FD4/0), 4% (FD4/4), 8% (FD4/8) (group I) and 12% (FD4/12) or 16% (FD4/16) (group II); the diets were given for 2 weeks each. Comparing diet FD4/0 to FD4/16, enrichment of α-linolenic acid was greatest in cholesteryl esters (+6.8% in plasma, +7.1% in low density lipoproteins (LDL), +5.9% in high density lipoproteins (HDL)), less in phosphatidylcholine (+2.5% in plasma, +2.9% in LDL, +2.7% in HDL), and least in platelet lipids (+0.7%). The accumulation of α-linolenic acid was compensated by a decrease of oleic acid. Eicosapentaenoic acid (EPA), which was excluded from the diet, increased in all plasma lipids with augmented α-linolenic acid intake, indicating a chain elongation and desaturation of α-linolenic acid to EPA. However, even at the end of FD4/16, EPA was less than 2% of total fatty acids in all plasma lipids. Plasma linoleic acid levels were constant during all dietary regimes, according to the constant dietary intake of this fatty acid. No replacement of linoleic acid by α-linolenic acid could be observed. The percentage of arachidonic acid in all lipids was unaffected by α-linolenic acid intake. As arachidonic acid was not provided by the diet, it can be concluded that α-linolenic acid does not inhibit chain elongation and desaturation of linoleic acid to arachidonic acid in man. Fatty acids in platelet lipids, except for a small increase of α-linolenic acid and EPA, were barely affected by dietary manipulations. PG metabolites and PGE_2 decreased, −52% and −85%, respectively, in 24-hr urine specimens with increasing α-linolenic acid intake. $PGF_{2\alpha}$ was unaffected up to an α-linolenic acid intake of 8% of calories; thereafter a decrease (−74%), compared to the values during free diet, could be observed. The results of our experiment demonstrate that for α-linolenic acid there is a reduced incorporation into plasma and platelet lipids, and a slower transformation to higher unsaturated fatty acids, compared to the values found with linoleic acid. PG biosynthesis, but not the conversion of linoleic acid to arachidonic acid, is suppressed by α-linolenic acid ingestion.—**Adam, O., G. Wolfram, and N. Zöllner.** Effect of α-linolenic acid in the human diet on linoleic acid metabolism and prostaglandin biosynthesis. *J. Lipid Res.* 1986. **27:** 421–426.

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Modification of dietary fat alters the phospholipid fatty acid composition of plasma and cell membranes and thereby the availability of precursor substances for prostaglandin (PG) biosynthesis (1, 2). Moreover, there is a competition between dietary polyunsaturated fatty acids for desaturating and oxygenating enzymes, which until now has been demonstrated in vitro (3–5) and in animal experiments (6), but only for thromboxane in man (7). Linoleic (18:2, n-6) and α-linolenic (18:3, n-3) acids are the most abundant polyunsaturated fatty acids in Western diets. The same enzymatic systems that transform linoleic to arachidonic acid also transform α-linolenic acid to eicosapentaenoic acid (EPA) by identical metabolic steps of desaturation and chain elongation (8). α-Linolenic acid is a poor substrate for these enzymes and, in vitro, depresses the formation of arachidonic acid (9), by inhibition of the desaturating enzyme, and its conversion to PG (4), by inhibition of cyclooxygenase. Both effects may contribute to a depressed PG biosynthesis during α-linolenic acid feeding. To evaluate the effect of dietary α-linolenic acid on linoleic acid metabolism and PG biosynthesis in human subjects, a precise and constant intake of both fatty acids over a sufficient time period is necessary and the diet has to be devoid of arachidonic acid and EPA. To meet these requirements our experiments were done with liquid formula diets (FD).

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Abbreviations: FD, liquid formula diets; arachidonic acid, all-*cis* 5,8,11,14-eicosatetraenoic acid (20:4, n-6); CE cholesteryl esters; EPA, all-*cis* 5,8,11,14,17-eicosapentaenoic acid (20:5, n-3); GLC, gas–liquid chromatography; HDL, high density lipoproteins (density > 1.063 g/ml); LDL, low density lipoproteins (density 1.006–1.063 g/ml); linoleic acid, all-*cis* 9,12-octadecadienoic acid (18:2, n-6); linolenic acid, all-*cis* 9,12,15-octadecatrienoic acid (18:3, n-3); MS, mass spectrometry; PC, phosphatidylcholine; PE, phosphatidylethanolamine; PG, prostaglandin; TNPDA, tetranorprostanedioic acid.