Electronic Supplementary Material (ESI) for Food & Function.

Electronic Supplementary Information (ESI)

Table S1: Fatty acid profile of the linseed oil used in the study (own analysis).

Fatty acid	Common name	% of total fatty acids	rel. dev.[a] [%]
C14:0	Myristic acid	0.06	25.4
C15:0	Pentadecylic acid	0.03	31.4
C16:0	Palmitic acid	5.14	0.03
C16:1n7	Palmitoleic acid	0.05	4.71
C17:0	Margaric acid	0.06	1.45
C18:0	Stearic acid	4.23	0.09
C18:1n9	Oleic acid	15.2	0.03
C18:1n7	Vaccenic acid	0.65	0.33
C18:2n6	Linoleic acid	15.7	0.01
C19:0	Nonadecylic acid	0.12	0.46
C18:3n3	α-Linolenic acid	58.0	0.04
C20:0	Arachidic acid	0.17	0.76
C20:1n9	Icosenoic acid	0.11	1.69
C20:2n6	Eicosadienoic acid	0.03	18.6
C20:3n3	Eicosatrienoic acid	0.05	7.99
C22:0	Behenic acid	0.12	0.69
C24:0	Lignoceric acid	0.09	4.36
C22:6n3	Docosahexaenoic acid	0.19	1.07

[a] relative deviation from the mean

Table S2: LC-ESI-MS/MS analysis of free oxylipins in plasma.

Analyte	Mass transition m/z		Internal standard	LLOQ[a]	LLOQ[a]	Included in data analysis
	MS1	MS3	IS	Vial (nM)	500 µL Plasma (nM)	Plasma
20-OH-PGE_2	367.2	189.1	$^2H_4$-PGE_2	0.25	0.025	no, <LLOQ in 50% of samples
Δ^{17}-6-keto-$PGF_{1\alpha}$	367.2	163.2	$^2H_4$-6-keto-$PGF_{1\alpha}$	1.0	0.1	no, <LLOQ in 50% of samples
2,3-dinor-TxB_1	343.0	142.9	$^2H_4$-TxB_2	5.0	0.5	no, <LLOQ in 50% of samples
2,3-dinor-TxB_2	341.2	167.0	$^2H_4$-TxB_2	1.0	0.1	no, <LLOQ in 50% of samples
6-keto-PGF_{1a}	369.3	163.2	$^2H_4$-6-keto-$PGF_{1\alpha}$	1.8	0.1805	no, <LLOQ in 50% of samples
RvE1	349.3	195.0	$^2H_4$-TxB_2	1.2	0.12	no, <LLOQ in 50% of samples
20-COOH-LTB_4	365.2	347.2	$^2H_4$-TxB_2	1.0	0.1	no, <LLOQ in 50% of samples
TxB_3	367.3	169.3	$^2H_4$-TxB_2	0.25	0.025	yes
20-OH-LTB_4	351.2	195.2	$^2H_4$-PGD_2	0.25	0.025	no, <LLOQ in 50% of samples
13,14-dihydro-15-keto-tetranor-PGE_2	296.9	109.0	$^2H_4$-PGE_2	0.25	0.025	no, <LLOQ in 50% of samples
TxB_1	371.3	171.2	$^2H_4$-TxB_2	0.5	0.05	no, <LLOQ in 50% of samples
15-F_{2t}-IsoP (8-*iso*-$PGF_{2\alpha}$)	353.1	193.1	$^2H_4$-15-F_{2t}-IsoP	0.5	0.05	no, <LLOQ in 50% of samples
TXB_2	369.2	169.1	$^2H_4$-TxB_2	1.3	0.125	yes
11-dehydro-TxB_3	365.3	161.2	$^2H_4$-TxB_2	1.0	0.1	no, <LLOQ in 50% of samples
PGE_3	349.3	269.2	$^2H_4$-PGE_2	0.3	0.03	no, <LLOQ in 50% of samples
11β-$PGF_{2\alpha}$	353.3	193.1	$^2H_4$-PGE_2	0.5	0.05	no, <LLOQ in 50% of samples
5(*R*,*S*)-5-F_{2t}-IsoP (5-iP$F_{2\alpha}$-VI)	353.2	114.8	$^2H_{11}$-5(*R*,*S*)-5-F_{2t}-IsoP	0.5	0.05	no, <LLOQ in 50% of samples
PGD_3	349.3	269.2	$^2H_4$-PGD_2	1.0	0.1	no, <LLOQ in 50% of samples
$PGF_{1\alpha}$	355.4	293.2	$^2H_4$-PGE_2	0.25	0.025	no, <LLOQ in 50% of samples
PGE_2	351.2	271.3	$^2H_4$-PGE_2	0.25	0.025	yes
11-dehydro-TxB_2	367.0	161.1	$^2H_4$-TxB_2	0.50	0.05	no, <LLOQ in 50% of samples
PGE_1	353.3	317.2	$^2H_4$-PGE_2	0.33	0.0325	no, <LLOQ in 50% of samples
PGD_1	353.3	317.2	$^2H_4$-PGD_2	0.50	0.05	no, <LLOQ in 50% of samples
PGD_2	351.2	271.3	$^2H_4$-PGD_2	1.0	0.1	yes
15-keto-$PGF_{1\alpha}$	353.3	193.1	$^2H_4$-PGE_2	0.25	0.025	no, <LLOQ in 50% of samples
11,12,15-TriHETrE	353.2	167.1	$^2H_4$-PGE_2	0.50	0.05	no, <LLOQ in 50% of samples
LXA_4	351.2	115.2	$^2H_4$-PGE_2	0.18	0.0175	no, <LLOQ in 50% of samples
RvD1	375.3	141.0	$^2H_4$-PGE_2	0.25	0.025	no, <LLOQ in 50% of samples
13,14-dihydro-15-keto-$PGF_{2\alpha}$	353.3	183.3	$^2H_4$-PGE_2	0.50	0.05	yes
13,14-dihydro-15-keto-PGE_1	353.3	221.2	$^2H_4$-PGE_2	0.50	0.05	yes
dihomo-$PGF_{2\alpha}$	381.4	221.1	$^2H_4$-PGE_2	0.10	0.01	no, <LLOQ in 50% of samples
RvE2	333.2	253.3	$^2H_4$-PGE_2	2.0	0.2	no, <LLOQ in 50% of samples
PGJ_2	333.3	189.2	$^2H_4$-PGE_2	1.6	0.16	no, <LLOQ in 50% of samples
LTB_5	333.3	195.2	$^2H_4$-LTB_4	0.10	0.01	no, <LLOQ in 50% of samples
PGB_2	333.3	175.1	$^2H_4$-PGE_2	0.40	0.04	no, <LLOQ in 50% of samples
THF diol	353.2	127.1	$^2H_4$-LTB_4	0.25	0.025	no, <LLOQ in 50% of samples
18(*S*)-RvE3	333.2	201.3	$^2H_4$-PGE_2	1.0	0.1	no, <LLOQ in 50% of samples
12-OH-17(18)-EpETE	333.1	179.3	$^2H_4$-9,10-DiHOME	0.50	0.05	no, <LLOQ in 50% of samples
15,16-DiHODE	311.2	223.2	$^2H_4$-9,10-DiHOME	1.0	0.1	yes
9,10-DiHODE	311.2	201.2	$^2H_4$-9,10-DiHOME	0.20	0.02	yes
12,13-DiHODE	311.2	183.1	$^2H_4$-9,10-DiHOME	1.0	0.1	yes
8,15-DiHETE	335.2	235.2	$^2H_{11}$-14,15-DiHETrE	0.80	0.08	no, <LLOQ in 50% of samples
18(*R*)-RvE3	333.2	201.3	$^2H_4$-PGE_2	0.50	0.05	no, <LLOQ in 50% of samples
6-*trans*-LTB_4	335.2	195.1	$^2H_4$-LTB_4	0.50	0.05	no, <LLOQ in 50% of samples
5,15-DiHETE	335.3	173.2	$^2H_{11}$-14,15-DiHETrE	0.25	0.025	no, <LLOQ in 50% of samples
17,18-DiHETE	335.3	247.2	$^2H_{11}$-14,15-DiHETrE	0.25	0.025	yes
LTB_4	335.2	195.1	$^2H_4$-LTB_4	0.25	0.025	no, <LLOQ in 50% of samples
14,15-DiHETE	335.3	207.2	$^2H_{11}$-14,15-DiHETrE	0.25	0.025	yes
11,12-DiHETE	335.2	167.1	$^2H_{11}$-14,15-DiHETrE	0.25	0.025	yes
12,13-DiHOME	313.2	183.2	$^2H_4$-9,10-DiHOME	0.50	0.05	yes
8,9-DiHETE	335.2	127.1	$^2H_{11}$-14,15-DiHETrE	0.50	0.05	yes
9,10-DiHOME	313.2	201.2	$^2H_4$-9,10-DiHOME	0.50	0.05	yes
14,15-DiHETrE	337.2	207.1	$^2H_{11}$-14,15-DiHETrE	0.10	0.01	yes
19,20-DiHDPE	361.2	273.2	$^2H_{11}$-14,15-DiHETrE	0.50	0.05	yes

LTB_3	337.2	195.2	$^2H_4$-LTB_4	0.50	0.05	no, <LLOQ in 50% of samples
9,10-diH-stearic acid	315.0	170.8	$^2H_4$-9,10-DiHOME	2.0	0.2	yes
16,17-DiHDPE	361.2	233.2	$^2H_{11}$-14,15-DiHETrE	0.50	0.05	yes
11,12-DiHETrE	337.2	167.1	$^2H_{11}$-14,15-DiHETrE	0.25	0.025	yes
19-HEPE	317.2	229.3	$^2H_8$-12-HETE	0.71	0.071	yes
13,14-DiHDPE	361.2	193.2	$^2H_{11}$-14,15-DiHETrE	0.25	0.025	yes
20-HEPE	317.2	287.3	$^2H_8$-12-HETE	1.0	0.1	yes
9-HOTrE	293.2	171.2	$^2H_4$-9-HODE	0.50	0.05	yes
10,11-DiHDPE	361.2	153.2	$^2H_{11}$-14,15-DiHETrE	0.25	0.025	yes
8,9-DiHETrE	337.2	127.1	$^2H_{11}$-14,15-DiHETrE	0.50	0.05	yes
13-HOTrE	293.2	195.1	$^2H_4$-9-HODE	0.60	0.06	yes
18-HEPE	317.2	259.2	$^2H_4$-9-HODE	1.0	0.1	yes
15-deoxy-PGJ_2	315.2	271.2	$^2H_{11}$-14,15-DiHETrE	0.50	0.05	no, <LLOQ in 50% of samples
7,8-DiHDPE	361.2	113.1	$^2H_{11}$-14,15-DiHETrE	1.0	0.1	yes
20-HETE	319.2	289.1	$^2H_6$-20-HETE	1.0	0.1	yes
15-HEPE	317.2	219.2	$^2H_8$-12-HETE	1.3	0.125	yes
5,6-DiHETrE	337.2	145.1	$^2H_{11}$-14,15-DiHETrE	0.50	0.05	yes
11-HEPE	317.0	167.0	$^2H_8$-12-HETE	0.50	0.05	yes
8-HEPE	317.2	155.2	$^2H_8$-12-HETE	0.63	0.0625	yes
12-HEPE	317.2	179.2	$^2H_8$-12-HETE	0.63	0.0625	yes
9-HEPE	317.2	166.9	$^2H_8$-12-HETE	0.50	0.05	yes
21-HDHA	343.0	255.0	$^2H_8$-12-HETE	1.65	0.165	yes
5-HEPE	317.2	115.1	$^2H_8$-12-HETE	0.50	0.05	yes
22-HDHA	343.2	313.2	$^2H_8$-12-HETE	2.80	0.28	yes
4,5-DiHDPE	361.2	229.3	$^2H_{11}$-14,15-DiHETrE	2.0	0.2	yes
13-HODE	295.2	195.2	$^2H_4$-9-HODE	5.0	0.5	yes
9-HODE	295.2	171.1	$^2H_4$-9-HODE	5.0	0.5	yes
20-HDHA	343.2	241.201	$^2H_8$-12-HETE	0.50	0.05	yes
15(16)-EpODE	293.3	235.2	$^2H_4$-9(10)-EpOME	0.50	0.05	no[b]
15-HETE	319.2	219.2	$^2H_8$-12-HETE	1.3	0.125	yes
9(10)-EpODE	293.3	171.2	$^2H_4$-9(10)-EpOME	0.40	0.04	no[b]
17(18)-EpETE	317.2	215.2	$^2H_{11}$-14(15)-EpETrE	1.0	0.1	no[b]
16-HDHA	343.2	233.201	$^2H_8$-12-HETE	0.25	0.025	yes
17-HDHA	343.2	201.2	$^2H_8$-12-HETE	2.0	0.2	yes
13-HDHA	343.2	193.1	$^2H_8$-12-HETE	0.50	0.05	yes
12(13)-EpODE	293.2	183.1	$^2H_4$-9(10)-EpOME	0.50	0.05	no[b]
11-HETE	319.2	167.2	$^2H_8$-12-HETE	0.50	0.05	yes
10-HDHA	343.2	153.201	$^2H_8$-12-HETE	0.50	0.05	yes
14-HDHA	343.2	205.2	$^2H_8$-12-HETE	1.0	0.1	yes
14(15)-EpETE	317.2	207.2	$^2H_{11}$-14(15)-EpETrE	0.50	0.05	no[b]
8-HETE	319.2	155.2	$^2H_8$-12-HETE	1.3	0.125	yes
12-HETE	319.2	179.2	$^2H_8$-12-HETE	0.50	0.05	yes
11(12)-EpETE	317.2	167.2	$^2H_{11}$-14(15)-EpETrE	0.50	0.05	no[b]
11-HDHA	343.2	121.1	$^2H_8$-5-HETE	0.25	0.025	yes
7-HDHA	343.2	141.2	$^2H_8$-5-HETE	1.0	0.1	yes
8(9)-EpETE	317.2	127.2	$^2H_{11}$-14(15)-EpETrE	1.0	0.1	no[b]
9-HETE	319.2	167.2	$^2H_8$-5-HETE	2.5	0.25	yes
15(S)-HETrE	321.2	221.2	$^2H_8$-5-HETE	0.50	0.05	yes
8-HDHA	343.2	189.2	$^2H_8$-5-HETE	0.50	0.05	yes
5-HETE	319.2	115.2	$^2H_8$-5-HETE	0.50	0.05	yes
4-HDHA	343.2	101.1	$^2H_8$-5-HETE	0.25	0.025	yes
19(20)-EpDPE	343.2	241.2	$^2H_{11}$-14(15)-EpETrE	0.50	0.05	no[b]
12(13)-EpOME	295.3	195.2	$^2H_4$-9(10)-EpOME	0.25	0.025	no[b]
14(15)-EpETrE	319.2	219.3	$^2H_{11}$-14(15)-EpETrE	0.50	0.05	no[b]
9(10)-EpOME	295.3	171.1	$^2H_4$-9(10)-EpOME	0.25	0.025	no[b]
16(17)-EpDPE	343.2	233.2	$^2H_{11}$-14(15)-EpETrE	0.50	0.05	no[b]
13(14)-EpDPE	343.2	193.2	$^2H_{11}$-14(15)-EpETrE	0.50	0.05	no[b]
5-oxo-ETE	317.2	273.2	$^2H_4$-9(10)-EpOME	2.0	0.2	no, <LLOQ in 50% of samples
10(11)-EpDPE	343.2	153.2	$^2H_{11}$-14(15)-EpETrE	0.25	0.025	no[b]
11(12)-EpETrE	319.3	167.2	$^2H_{11}$-14(15)-EpETrE	0.50	0.05	no[b]
8(9)-EpETrE	319.2	155.2	$^2H_{11}$-14(15)-EpETrE	1.0	0.1	no[b]
5(6)-EpETrE	319.2	191.1	$^2H_{11}$-14(15)-EpETrE	2.0	0.2	no[b]

9(10)-ep-stearic acid	297.0	170.8	$^{2}H_{4}$-9(10)-EpOME	2.0	0.2	no[b]

Shown are the covered analytes, the mass transition used for quantification in scheduled selected reaction monitoring mode, the internal standard (IS) and the lower limit of quantification (LLOQ).

[a] LLOQ was set to the lowest calibration standard injected within the sample set yielding a signal to noise ratio ≤ 5 and accuracy in the calibration within ±20%.

[b] Epoxy-FA not included in data analysis due to high variation in quality control samples.

Table S3: Concentration and relative amount of fatty acids in red blood cells in the follow-up period.

	wk 14			t-test[a]	wk 20			t-test[a]	AnreM[b]
	mean	±	SE	p (wk 14 - wk 12)	mean	±	SE	p (wk 20 - wk 12)	p
C12:0 µg/mL	<0.25			-	<0.25			-	-
% of total FA	-			-	-			-	-
C14:0 µg/mL	3.08	±	0.18	-	3.14	±	0.18	-	n.s.
% of total FA	0.31	±	0.02	-	0.32	±	0.01	-	n.s.
C14:1n5 µg/mL	<0.25			-	<0.25			-	-
% of total FA	-			-	-			-	-
C15:0 µg/mL	1.65	±	0.08	n.s.	1.67	±	0.07	n.s.	**0.047**
% of total FA	0.17	±	0.01	-	0.17	±	0.01	-	n.s.
C16:0 µg/mL	191	±	6.09	-	194	±	5.01	-	n.s.
% of total FA	19.7	±	0.11	-	19.7	±	0.19	-	n.s.
C16:1n7 µg/mL	2.64	±	0.20	-	2.79	±	0.28	-	n.s.
% of total FA	0.27	±	0.02	-	0.28	±	0.02	-	n.s.
C17:0 µg/mL	3.08	±	0.09	n.s.	3.19	±	0.12	n.s.	**0.043**
% of total FA	0.32	±	0.01	**0.020**	0.32	±	0.01	n.s.	**0.028**
C18:0 µg/mL	149	±	3.67	-	150	±	2.88	-	n.s.
% of total FA	15.4	±	0.12	n.s.	15.3	±	0.11	n.s.	**0.039**
C18:1n9 µg/mL	123	±	4.99	-	127	±	4.78	-	n.s.
% of total FA	12.6	±	0.20	-	12.9	±	0.23	-	n.s.
C18:1n7 µg/mL	13.1	±	0.49	-	13.4	±	0.46	-	n.s.
% of total FA	1.35	±	0.02	-	1.36	±	0.02	-	**0.032**
C18:2n6 µg/mL	97.8	±	3.73	-	98.4	±	3.76	-	n.s.
% of total FA	10.1	±	0.33	n.s.	10.1	±	0.37	**0.004**	**0.001**
C18:3n6 µg/mL	<0.25			-	<0.25			-	-
% of total FA	-			-	-			-	-
C19:0 µg/mL	<0.25			-	<0.25			-	-
% of total FA	-			-	-			-	-
C18:3n3 µg/mL	2.62	±	0.16	**<0.001**	2.27	±	0.21	**<0.001**	**<0.001**
% of total FA	0.27	±	0.01	**<0.001**	0.23	±	0.02	**<0.001**	**<0.001**
C20:0 µg/mL	4.60	±	0.21	**0.006**	4.57	±	0.19	**0.032**	**0.011**
% of total FA	0.48	±	0.02	n.s.	0.46	±	0.01	**0.039**	**0.045**
C20:1n9 µg/mL	2.95	±	0.12	n.s.	3.03	±	0.15	n.s.	**0.047**
% of total FA	0.30	±	0.01	-	0.31	±	0.01	-	n.s.
C20:2n6 µg/mL	1.98	±	0.12	-	2.13	±	0.15	-	n.s.
% of total FA	0.21	±	0.01	-	0.22	±	0.01	-	n.s.
C20:3n6 µg/mL	14.3	±	1.05	**0.43**	16.4	±	0.93	**0.001**	**<0.001**
% of total FA	1.47	±	0.09	**0.043**	1.67	±	0.09	**<0.001**	**<0.001**
C20:4n6 µg/mL	136	±	4.17	n.s.	139	±	3.45	n.s.	**0.023**
% of total FA	14.0	±	0.15	**0.012**	14.2	±	0.15	**0.001**	**<0.001**
C20:5n3 µg/mL	10.0	±	0.52	**0.009**	8.53	±	0.69	**<0.001**	**<0.001**
% of total FA	1.03	±	0.04	**0.002**	0.87	±	0.06	**<0.001**	**<0.001**
C22:0 µg/mL	17.0	±	0.53	n.s.	16.5	±	0.46	n.s.	**0.046**
% of total FA	1.76	±	0.04	**0.006**	1.68	±	0.03	n.s.	**0.004**

C22:1n9 µg/mL	2.18	±	0.17	-	1.72	±	0.20	-	n.s.
% of total FA	0.23	±	0.02	-	0.17	±	0.02	-	n.s.
C22:4n6 µg/mL	26.5	±	0.99	n.s.	28.3	±	1.00	n.s.	**0.035**
% of total FA	2.74	±	0.06	n.s.	2.87	±	0.08	n.s.	**<0.001**
C22:5n3 µg/mL	35.3	±	1.63	-	32.6	±	1.49	-	n.s.
% of total FA	3.64	±	0.12	n.s.	3.31	±	0.11	n.s.	**0.001**
C24:0 µg/mL	48.2	±	1.24	n.s.	47.8	±	1.15	n.s.	**0.077**
% of total FA	5.00	±	0.10	-	4.87	±	0.08	-	n.s.
C22:6n3 µg/mL	32.8	±	1.15	-	33.8	±	1.57	-	n.s.
% of total FA	3.41	±	0.13	-	3.46	±	0.17	-	n.s.
C24:1n9 µg/mL	50.5	±	1.84	n.s.	52.0	±	1.69	-	**0.008**
% of total FA	5.21	±	0.09	**0.012**	5.28	±	0.09	**0.003**	**0.001**
TFA µg/mL	969	±	27.4	-	984	±	22.3	-	n.s.
SFA µg/mL	417	±	11.2	-	421	±	9.18	-	n.s.
% of total FA	43.1	±	0.17	-	42.9	±	0.14	-	n.s.
MUFA µg/mL	194	±	7.27	-	200	±	7.05	-	n.s.
% of total FA	20.0	±	0.28	**0.002**	20.3	±	0.31	n.s.	**0.001**
PUFA µg/mL	357	±	9.63	-	362	±	7.16	-	n.s.
% of total FA	37.0	±	0.23	n.s.	36.9	±	0.32	**0.023**	**0.012**
Σn3 PUFA µg/mL	80.7	±	2.47	-	77.2	±	2.60	-	n.s.
% of total FA	8.35	±	0.15	**0.009**	7.86	±	0.22	**0.001**	**<0.001**
Σn6 PUFA µg/mL	277	±	7.82	-	285	±	5.98	-	n.s.
% of total FA	28.6	±	0.28	n.s.	29.0	±	0.33	**0.050**	**0.018**
ΣEPADHA µg/mL	42.9	±	1.44	-	42.3	±	1.88	-	n.s.
% of total FA	4.45	±	0.14	-	4.32	±	0.20	-	n.s.
Σ n6/Σ n3 PUFA	3.44	±	0.08	**0.014**	3.73	±	0.13	**0.002**	**<0.001**
AA/EPA	13.8	±	0.47	**<0.001**	17.3	±	1.06	**<0.001**	**<0.001**
D5D index	10.1	±	0.60	n.s.	8.75	±	0.45	**0.001**	**0.002**
D6D index	0.15	±	0.01	**0.006**	0.17	±	0.01	**<0.001**	**<0.001**
% n3 in HUFA	30.7	±	0.39	n.s.	28.9	±	0.63	**<0.001**	**<0.001**
% n6 in HUFA	69.3	±	0.39	n.s.	71.1	±	0.63	**<0.001**	**<0.001**

Levels are shown as concentration [µg/mL] in blood and as relative amount [%] of total fatty acids at wk 14 and wk 20 (2 and 8 weeks after completion of the 12-week intervention).
AA: arachidonic acid; D5D/D6D index, delta-5/6 desaturase index: calculated according to (Bokor et al., 2010): D5D=C20:4n6/C20:3n6 and D6D=C20:3n6/C18:2n6; EPA: eicosapentaenoic acid; HUFA: highly unsaturated fatty acids; indices of HUFA calculated as follows, modified from Lands (2008): % n3 in HUFA = 100*(C20:5n3 + C22:5n3 + C22:6n3)/(C20:3n6 + C20:4n6 + C22:4n6 + C20:5n3 + C22:5n3 + C22:6n3); % n6 in HUFA = 100*(C20:3n6 + C20:4n6 + C22:4n6)/(C20:3n6 + C20:4n6 + C22:4n6 + C20:5n3 + C22:5n3 + C22:6n3); MUFA: monounsaturated fatty acids: C14:1n5, C15:1n5, C16:1n7, C17:1n7, C18:1n9, C18:1n7, C20:1n9, C22:1n9, 24:1n9; n.s.: not significant; SFA: saturated fatty acids: C10:0, C11:0, C12:0, C13:0, C14:0, C15:0, C16:0, C17:0, C18:0, C20:0, C21:0, C22:0, C24:0; PUFA: polyunsaturated fatty acids: C18:2n6, C18:3n6, C18:3n3, C20:2n6, C20:3n6, C20:4n6, C20:5n3, C22:4n6, C22:5n3, C22:6n3; SE: standard error; TFA: total fatty acids; Σ n3 PUFA: C18:3n3, C20:3n3, C20:5n3, C22:5n3, C22:6n3; Σ n6 PUFA: C18:2n6, C18:3n6, C20:2n6, C20:3n6, C20:4n6, C22:2n6, C22:4n6; wk: week.
[a] t-test for paired samples with Holm-Bonferroni correction; significance level p≤0.05
[b] ANOVA for repeated measures (An reM); significance level p≤0.05

Table S4: Concentration of free oxylipins (pM) in plasma.

	wk 0			wk 1			t-test[a]	wk 3			t-test[a]	wk 6			t-test[a]	wk 12			t-test[a]	An reM[b]
	mean	±	SE	mean	±	SE	p (wk 1-0)	mean	±	SE	p (wk 3-0)	mean	±	SE	p (wk 6-0)	mean	±	SE	p (wk 12-0)	p
ALA-oxylipins																				
Hydroxy fatty acids																				
9-HOTrE	693	±	71.7	814	±	58.5	n.s.	897	±	88.0	n.s.	1141	±	127	**0.021**	1285	±	106	**0.001**	**<0.001**
13-HOTrE	993	±	113	1384	±	109	n.s.	1888	±	165	**0.001**	1990	±	256	**0.008**	2569	±	234	**<0.001**	**<0.001**
Dihydroxy fatty acids																				
9,10-DiHODE	403	±	142	280	±	23.0	-	291	±	27.9	-	405	±	81.3	-	579	±	253	-	n.s.
12,13-DiHODE	284	±	33.7	282	±	18.9	n.s.	295	±	17.5	n.s.	414	±	48.8	n.s.	380	±	31.9	**0.017**	**0.001**
15,16-DiHODE	18243	±	2970	19895	±	1804	n.s.	21065	±	2057	n.s.	28086	±	3631	n.s.	24795	±	1802	**0.033**	**0.007**
EPA-oxylipins																				
Hydroxy fatty acids																				
5-HEPE	160	±	22.2	134	±	8.42	-	161	±	11.6	-	238	±	52.4	-	200	±	13.5	-	n.s.
8-HEPE	<LLOQ			<LLOQ				<LLOQ			-	144	±	61.6	-	94.70	±	5.59	-	-
12-HEPE[c]	6032	±	1108	3590	±	471	n.s.	11064	±	1081	**0.030**	5790	±	814	n.s.	16534	±	1701	**<0.001**	**<0.001**
15-HEPE	156	±	10.3	175	±	12.5	n.s.	199	±	13.4	**0.030**	211	±	18.0	**0.040**	230	±	22.3	**0.033**	**<0.001**
18-HEPE	203	±	21.5	231	±	12.1	n.s.	247	±	13.8	n.s.	348	±	30.9	**0.002**	317	±	22.0	**0.001**	**<0.001**
19-HEPE	747	±	113	929	±	63.2	n.s.	1057	±	127	n.s.	1272	±	199	n.s.	1082	±	104	n.s.	**0.005**
20-HEPE	429	±	72.1	463	±	31.4	-	457	±	33.0	-	557	±	64.8	-	492	±	49.5	-	n.s.
Dihydroxy fatty acids																				
8,9-DiHETE	<LLOQ			67.4	±	3.23	-	71.1	±	5.01	-	92.1	±	12.6	-	80.0	±	5.97	-	**-**
11,12-DiHETE	42.8	±	5.71	47.4	±	2.52	n.s.	53.7	±	3.35	n.s.	68.9	±	7.41	n.s.	64.7	±	4.21	**0.008**	**<0.001**
14,15-DiHETE	88.3	±	9.94	100	±	5.01	n.s.	111	±	6.44	n.s.	142	±	15.7	**0.032**	125	±	7.23	**0.006**	**<0.001**
17,18-DiHETE	537	±	65.4	690	±	41.3	n.s.	760	±	56.1	**0.045**	946	±	95.7	**0.006**	854	±	53.7	**0.001**	**<0.001**
DHA-oxylipins																				
Hydroxy fatty acids																				
4-HDHA	284	±	42.0	230	±	22.8	n.s.	197	±	18.9	n.s.	375	±	46.3	n.s.	305	±	24.3	n.s.	**0.002**
7-HDHA	151	±	13.3	133	±	10.6	n.s.	158	±	16.2	n.s.	243	±	54.3	n.s.	227	±	16.1	**0.001**	**0.007**
8-HDHA	439	±	55.2	380	±	39.7	n.s.	416	±	40.4	n.s.	787	±	148	n.s.	627	±	44.4	**0.024**	**<0.001**

10-HDHA	273	±	30.1	184	±	18.0	n.s.	318	±	30.5	n.s.	323	±	80.4	n.s.	380	±	31.5	n.s.	**0.014**
11-HDHA	8962	±	1111	4265	±	550	**0.004**	10903	±	1313	n.s.	5677	±	819	n.s.	12049	±	1064	n.s.	**<0.001**
13-HDHA	167	±	20.1	122	±	12.2	n.s.	151	±	13.2	n.s.	200	±	33.9	n.s.	206	±	15.9	n.s.	**0.010**
14-HDHA[c]	9910	±	1114	5058	±	621	**0.004**	13189	±	1349	n.s.	6846	±	1026	n.s.	15098	±	1405	**0.016**	**<0.001**
16-HDHA	173	±	13.9	156	±	13.9	n.s.	147	±	9.21	n.s.	227	±	39.1	n.s.	172	±	9.35	n.s.	**0.038**
17-HDHA	774	±	82.9	658	±	80.9	-	756	±	91.6	-	868	±	136	-	882	±	84.6	-	n.s.
20-HDHA	423	±	39.2	367	±	28.0	-	372	±	24.3	-	455	±	64.6	-	351	±	20.3	-	n.s.
21-HDHA	2098	±	218	1692	±	148	-	1661	±	89.4	-	1806	±	255	-	1438	±	103	-	n.s.
22-HDHA	2283	±	308.3	1731	±	160	n.s.	1757	±	116	n.s.	1909	±	254	n.s.	1480	±	114	n.s.	**0.039**
Dihydroxy fatty acids																				
4,5-DiHDPE	696	±	76.6	540	±	50.6	-	502	±	24.2	-	717	±	169	-	492	±	32.5	-	n.s.
7,8-DiHDPE	<LLOQ			<LLOQ			-	<LLOQ			-	<LLOQ			-	<LLOQ			-	-
10,11-DiHDPE	188	±	29.3	128	±	14.7	n.s.	124	±	8.52	n.s.	150	±	23.9	n.s.	111	±	7.76	n.s.	**0.029**
13,14-DiHDPE	232	±	23.3	184	±	13.5	n.s.	182	±	10.6	n.s.	189	±	15.2	n.s.	162	±	8.84	n.s.	**0.008**
16,17-DiHDPE	321	±	32.2	254	±	15.3	n.s.	256	±	16.6	n.s.	284	±	32.0	n.s.	227	±	14.7	n.s.	**0.047**
19,20-DiHDPE	2958	±	383	2318	±	199	-	2310	±	165	-	2337	±	219	-	2006	±	138	-	n.s.
LA-Oxylipins																				
Hydroxy fatty acids																				
9-HODE	13621	±	1868	11311	±	856	-	11169	±	757	-	12594	±	1021	-	13625	±	1746	-	n.s.
13-HODE	20227	±	2952	14821	±	1201	-	15538	±	1103	-	15725	±	1209	-	19240	±	2855	-	n.s.
Dihydroxy fatty acids																				
9,10-DiHOME	5276	±	764	4019	±	584	-	4002	±	551	-	4625	±	668	-	6091	±	2161	-	n.s.
12,13-DiHOME	5998	±	654	4355	±	384	n.s.	4253	±	313	n.s.	5343	±	444	n.s.	5038	±	465	n.s.	**0.010**
AA-oxylipins																				
Thromboxanes, prostaglandins																				
PGD2	<LLOQ			<LLOQ				<LLOQ				<LLOQ				<LLOQ				
PGE2	81.7	±	14.8	35.3	±	2.58	n.s.	57.9	±	7.52	n.s.	47.9	±	6.51	n.s.	90.0	±	9.40	n.s.	**<0.001**
13,14-dihydro-15-keto-PGF2a	136	±	7.46	130	±	7.01	-	136	±	8.35	-	156	±	9.12	-	147	±	8.81	-	n.s.
TXB2	477	±	58.7	293	±	16.2	n.s.	418	±	45.3	n.s.	387	±	45.6	n.s.	660	±	57.3	n.s.	**<0.001**
TXB3	<LLOQ			<LLOQ			-	44.7	±	4.74	-	56.3	±	9.34	-	<LLOQ			-	**-**

13,14-dihydro-15-keto-PGE1	125	±	24.7	<LLOQ			-	110	±	21.8	-	<LLOQ			-	115	±	27.1	-	n.s.
Hydroxy fatty acids																				
5-HETE	550	±	70.4	413	±	21.9	-	408	±	28.4	-	476	±	25.0	-	474	±	32.5	-	n.s.
8-HETE	317	±	23.1	256	±	16.4	n.s.	326	±	17.5	n.s.	325	±	16.4	n.s.	390	±	24.9	n.s.	**0.001**
9-HETE	<LLOQ			<LLOQ			-	<LLOQ			-	<LLOQ			-	<LLOQ			-	-
11-HETE	261	±	21.2	213	±	12.5	-	233	±	11.2	-	266	±	12.3	-	310	±	18.8	-	n.s.
12-HETE[c]	18479	±	2315	9146	±	873	**0.015**	24454	±	2148	n.s.	10471	±	1135	n.s.	29175	±	2434	**0.005**	**<0.001**
15-HETE	864	±	72.8	751	±	40.4	-	838	±	45.3	-	795	±	35.8	-	872	±	58.2	-	n.s.
20-HETE	896	±	160	654	±	57.3	-	693	±	61.7	-	652	±	41.3	-	672	±	40.4	-	n.s.
Dihydroxy fatty acids																				
5,6-DiHETrE	220	±	24.0	182	±	10.0	n.s.	181	±	11.2	n.s.	177	±	8.44	n.s.	173	±	10.2	n.s.	**0.044**
8,9-DiHETrE	247	±	22.0	201	±	12.4	n.s.	201	±	10.5	n.s.	200	±	8.89	n.s.	194	±	8.83	n.s.	**0.024**
11,12-DiHETrE	611	±	52.5	492	±	29.0	n.s.	516	±	25.7	n.s.	494	±	17.9	n.s.	490	±	21.1	n.s.	**0.016**
14,15-DiHETrE	727	±	59.0	611	±	25.7	n.s.	626	±	26.8	n.s.	608	±	16.4	n.s.	600	±	21.8	n.s.	**0.044**
DGLA-Oxylipins																				
Hydroxy fatty acids																				
15(S)-HETrE	268	±	17.7	245	±	14.3	-	258	±	16.5	-	282	±	11.2	-	292	±	14.5	-	n.s.

Levels are shown at wk 0, 1, 3, 6, and 12 of high ALA diet (14.0±0.45 g/d).
DiHDPE: dihydroxy docosapentaenoic acid; DiHETE: dihydroxy eicosatetraenoic acid; DiHETrE: dihydroxy eicosatrienoic acid; DiHODE: dihydroxy octadecadienoic acid; DiHOME: dihydroxy octadecenoic acid; HDHA: hydroxy docosahexaenoic acid; HETrE: hydroxy eicosatrienoic acid; HEPE: hydroxy eicosapentaenoic acid; HETE: hydroxy eicosatetraenoic acid; HODE: hydroxy octadecadienoic acid; HOTrE: hydroxy octadecatrienoic acid; LLOQ: lower limit of quantification; n.s.: not significant; PG: prostaglandin; SE: standard error; TX: Thromboxane; wk: week.
[a] t-test for paired samples with Holm-Bonferroni correction; significance level p≤0.05
[b] ANOVA for repeated measures (An reM); significance level p≤0.05
[c] 12-LOX metabolites: highly variable concentration in quality control samples, most likely due to residual enzyme activity

Table S5: Concentration of free oxylipins (pM) in the follow-up period.

	wk 14			t-test[a]	wk 20			t-test[a]	An reM[b]
	mean	±	SE	p (wk 14 - wk 12)	mean	±	SE	p (wk 20 - wk 12)	p
ALA-Oxylipins									
Hydroxy fatty acids									
9-HOTrE	834	±	78.6	**0.015**	914	±	102	n.s.	**0.011**
13-HOTrE	1195	±	109	**0.002**	980	±	116	**0.002**	**<0.001**
Dihydroxy fatty acids									
9,10-DiHODE	248	±	32.8	-	268	±	31.7	-	n.s.
12,13-DiHODE	277	±	30.7	**0.014**	299	±	34.7	n.s.	**0.009**
15,16-DiHODE	18892	±	2417	n.s.	18880	±	2449	n.s.	**0.043**
EPA-oxylipins									
Hydroxy fatty acids									
5-HEPE	187	±	13.5	-	179	±	26.2	-	n.s.
8-HEPE	81.8	±	5.89	-	78.5	±	7.67	-	n.s.
12-HEPE[c]	5921	±	861	**<0.001**	1896	±	387	**<0.001**	**<0.001**
15-HEPE	159	±	7.81	**0.012**	<LLOQ				**0.012**
18-HEPE	265	±	10.7	-	265	±	44.0	-	n.s.
19-HEPE	949	±	77.8	-	825	±	145	-	n.s.
20-HEPE	449	±	36.5	-	444	±	63.9	-	n.s.
Dihydroxy fatty acids									
8,9-DiHETE	64.7	±	3.65	-	64.6	±	8.52	-	n.s.
11,12-DiHETE	48.2	±	2.46	**0.006**	46.9	±	7.02	n.s.	**0.031**
14,15-DiHETE	97.1	±	5.20	**0.025**	88.5	±	9.26	**0.011**	**0.002**
17,18-DiHETE	635	±	41.4	**0.013**	594	±	76.0	**0.005**	**0.001**
DHA-oxylipins									
Hydroxy fatty acids									
4-HDHA	364	±	28.0	-	320	±	60.7	-	n.s.
7-HDHA	175	±	15.6	**0.042**	142	±	23.6	**0.037**	**0.013**
8-HDHA	575	±	42.6	-	508	±	104	-	n.s.
10-HDHA	264	±	24.4	**0.006**	172	±	22.8	**0.001**	**<0.001**
11-HDHA	5844	±	859	**0.001**	2309	±	452	**<0.001**	**<0.001**
13-HDHA	180	±	13.6	-	134	±	24.0	-	n.s.
14-HDHA[c]	7582	±	1085	**0.001**	3049	±	566	**<0.001**	**<0.001**
16-HDHA	200	±	10.6	-	182	±	23.9	-	n.s.
17-HDHA	718	±	83.2	n.s.	544	±	78.0	n.s.	**0.018**
20-HDHA	448	±	30.0	-	408	±	49.9	-	n.s.
21-HDHA	1942	±	149	-	1972	±	245	-	n.s.
22-HDHA	2027	±	164	-	1995	±	258	-	n.s.
Dihydroxy fatty acids									
4,5-DiHDPE	632	±	56.9	-	653	±	105	-	n.s.
7,8-DiHDPE	<LLOQ			-	<LLOQ			-	-
10,11-DiHDPE	139	±	11.3	-	145	±	22.2	-	n.s.
13,14-DiHDPE	195	±	11.3	-	191	±	19.9	-	n.s.
16,17-DiHDPE	268	±	12.9	-	257	±	21.8	-	n.s.
19,20-DiHDPE	2502	±	147	-	2391	±	255	-	n.s.
LA-Oxylipins									
Hydroxy fatty acids									

9-HODE	11374	±	964	-	12350	±	1728	-	n.s.
13-HODE	14322	±	1271	-	14998	±	1906	-	n.s.
Dihydroxy fatty acids									
9,10-DiHOME	4114	±	771	-	4792	±	1035	-	n.s.
12,13-DiHOME	4628	±	556	-	5309	±	641	-	n.s.
AA-oxylipins									
Thromboxanes, prostaglandins									
PGD2	<LLOQ			-	<LLOQ			-	-
PGE2	74.7	±	6.97	-	<LLOQ			-	n.s.
13,14-dihydro-15-keto-PGF2a	147	±	11.8	-	159	±	14.0	-	n.s.
TXB2	539	±	44.4	-	2689	±	2447	-	n.s.
TXB3	67.6	±	6.83	-	64.6	±	30.7	-	n.s.
13,14-dihydro-15-keto-PGE1	<LLOQ				93.8	±	16.6	-	n.s.
Hydroxy fatty acids									
5-HETE	561	±	42.0	-	532	±	75.4	-	n.s.
8-HETE	332	±	16.4	-	289	±	29.9	-	n.s.
9-HETE	<LLOQ			-	<LLOQ			-	-
11-HETE	288	±	12.0	-	329	±	96.3	-	n.s.
12-HETE[c]	13790	±	1645	**<0.001**	6266	±	925	**<0.001**	**<0.001**
15-HETE	890	±	54.3	-	861	±	115	-	n.s.
20-HETE	839	±	62.0	-	762	±	86.0	-	n.s.
Dihydroxy fatty acids									
5,6-DiHETrE	204	±	11.5	-	210	±	19.2	-	n.s.
8,9-DiHETrE	228	±	10.1	-	240	±	22.0	-	n.s.
11,12-DiHETrE	556	±	26.8	-	556	±	40.3	-	n.s.
14,15-DiHETrE	662	±	22.7	-	660	±	37.6	-	n.s.
DGLA-Oxylipins									
Hydroxy fatty acids									
15(S)-HETrE	271	±	16.7	-	291	±	24.5	-	n.s.

Levels are shown at wk 14 and wk 20 (2 and 8 weeks after completion of the 12-week intervention).
DiHDPE: dihydroxy docosapentaenoic acid; DiHETE: dihydroxy eicosatetraenoic acid; DiHETrE: dihydroxy eicosatrienoic acid; DiHODE: dihydroxy octadecadienoic acid; DiHOME: dihydroxy octadecenoic acid; HDHA: hydroxy docosahexaenoic acid; HETrE: hydroxy eicosatrienoic acid; HEPE: hydroxy eicosapentaenoic acid; HETE: hydroxy eicosatetraenoic acid; HODE: hydroxy octadecadienoic acid; HOTrE: hydroxy octadecatrienoic acid; n.s.: not significant; PG: prostaglandin; SE: standard error; TX: Thromboxane; wk: week.
[a] t-test for paired samples with Holm-Bonferroni correction
[b] ANOVA for repeated measures (An reM) wk 12, wk 14 and wk 20; significance level $p \leq 0.05$
[c] 12-LOX metabolites: highly variable concentration in quality control samples, most likely due to residual enzyme activity