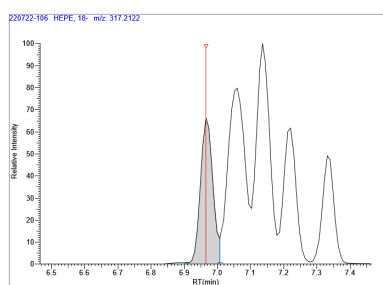
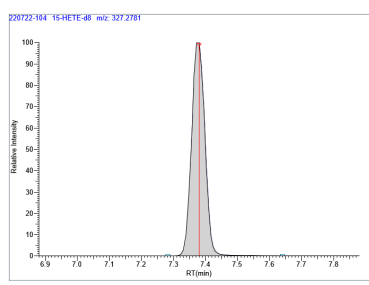


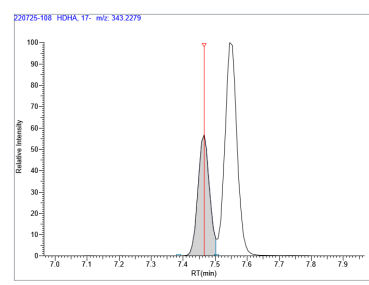
# Evaluation of the metabolite profile of Fish Oil Omega-3 fatty acids (n-3 FAs) in Micellar and Enteric Coated Forms – A Randomized, Cross-Over Human Study: Supplementary Data



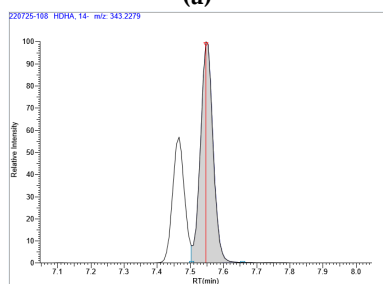
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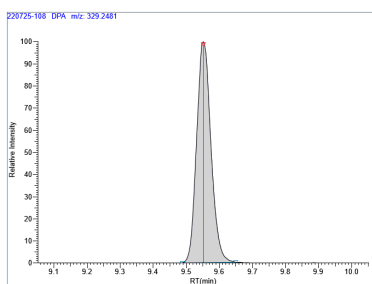
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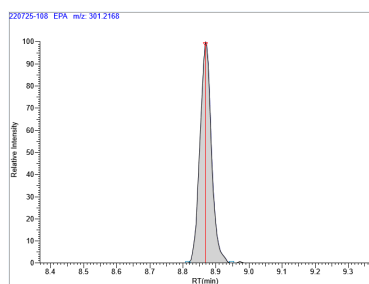
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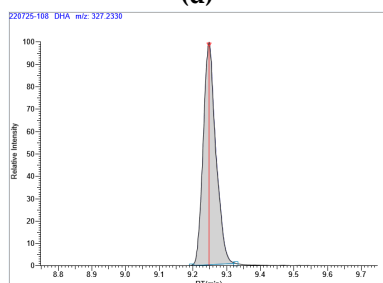
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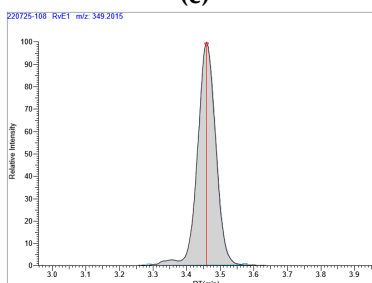
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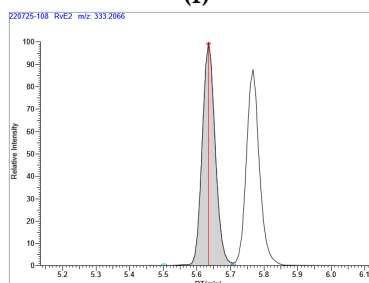
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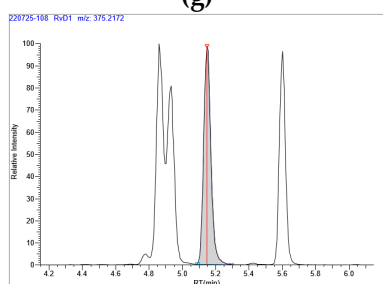
(g)



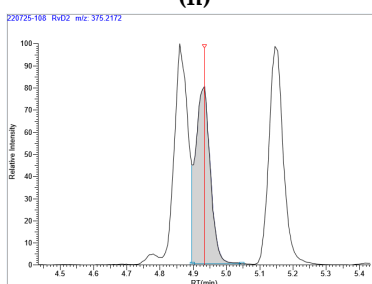
(h)



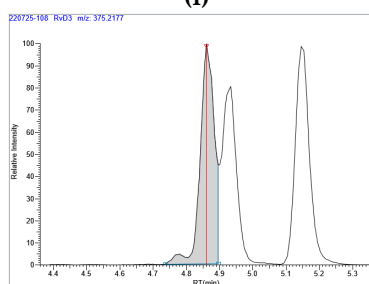
(i)



(j)



(k)



(l)

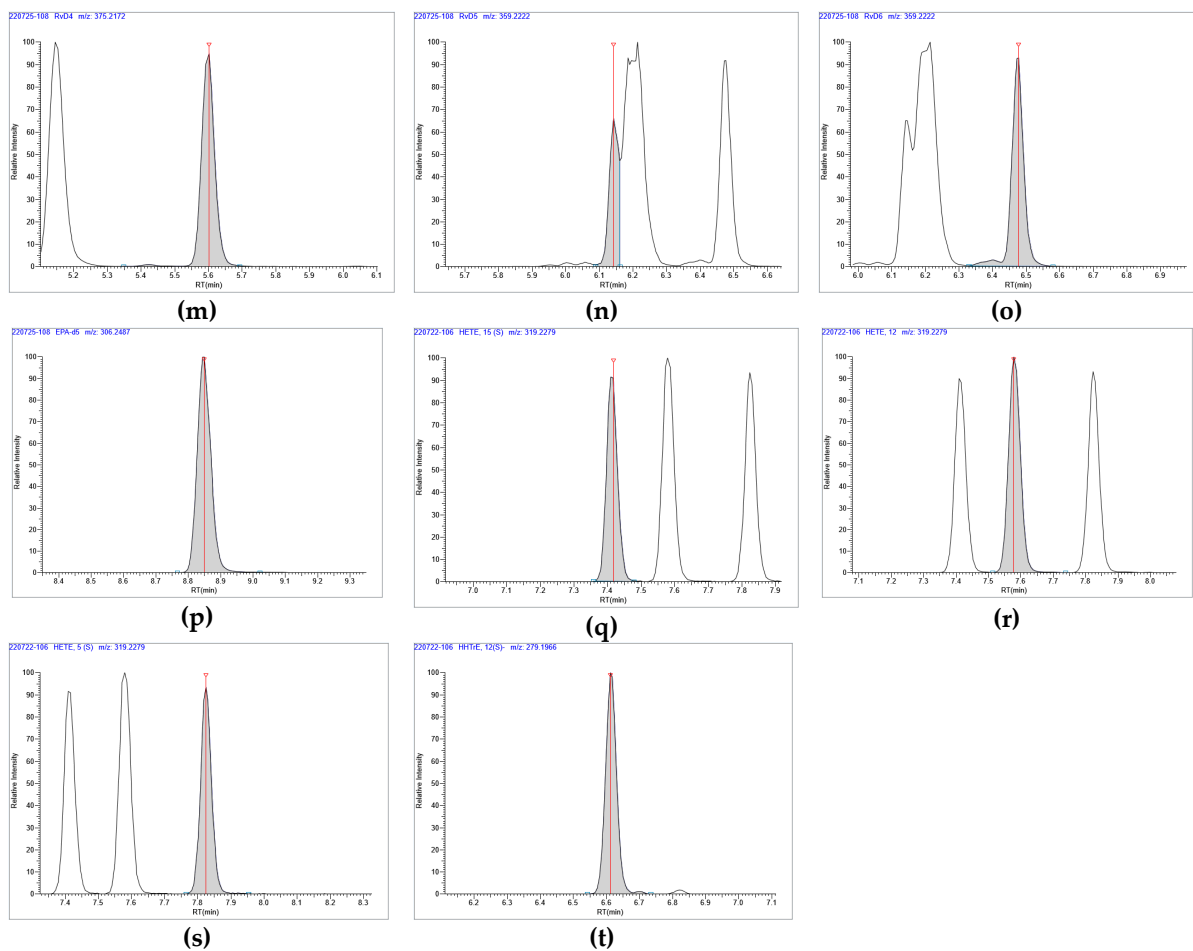
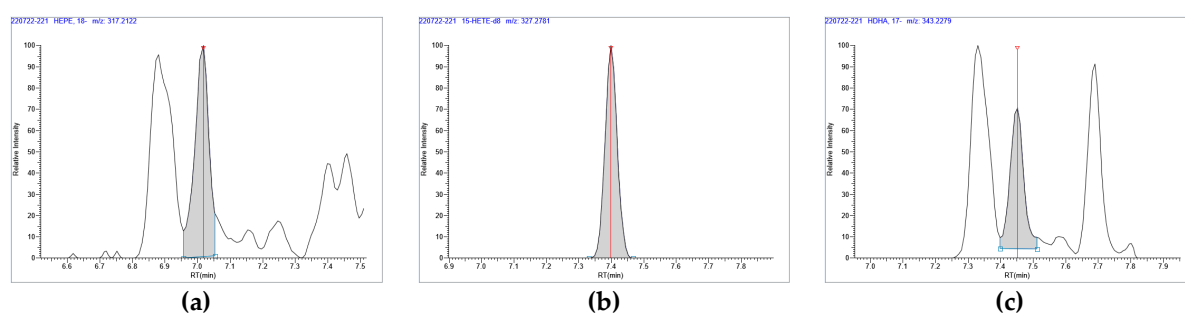


Figure S1: LC-HRMS chromatograms of n3-FAs and their metabolites. (a) 18-HEPE, (b) 15-HETE-d8, (c) 17-HDHA, (d) 14-HDHA, (e) DPA, (f) EPA, (g) DHA, (h) RvE1, (i) RvE2, (j) RvD1, (k) RvD2, (l) RvD3, (m) RvD4, (n) RvD5, (o) RvD6, (p) EPA-d5, (q) 15(S)-HETE, (r) 12(S)-HETE, (s) 5(S)-HETE, (t) 12(S)-HHTrE



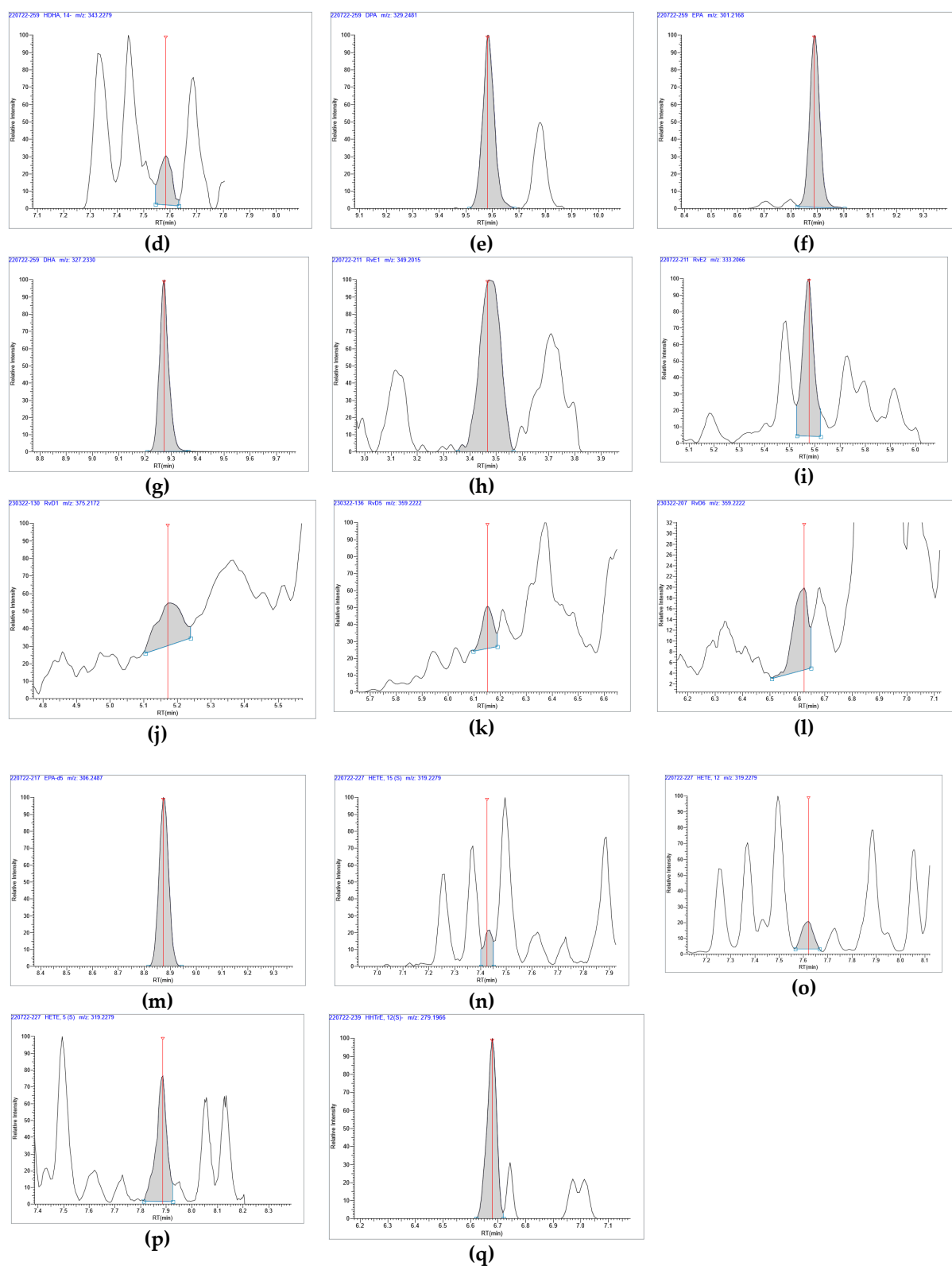


Figure S2: LC-HRMS chromatograms of n3-FAs and their metabolites as detected in participants' blood samples. (a) 18-HEPE, (b) 15-HETE-d8, (c) 17-HDHA, (d) 14-HDHA, (e) DPA, (f) EPA, (g) DHA, (h) RvE1,

(i) RvE2, (j) RvD1, (k) RvD5, (l) RvD6, (m) EPA-d5, (n) 15(S)-HETE, (o) 12(S)-HETE, (p) 5(S)-HETE, (q) 12(S)-HHTrE.

Table S1. HRMS data extraction parameters for n-3 FA and their metabolites

Compound Name	Compound Formula	Adduct	Retention Time
10-HDHA	C22H32O3	M-H	7.53
11-HDHA	C22H32O3	M-H	7.60
11-HEPE	C20H30O3	M-H	7.09
12(S)-HEPE	C20H30O3	M-H	7.25
12(S)-HETE	C20H32O3	M-H	7.60
12(S)-HHTrE	C17H28O3	M-H	6.66
14(s)-HDHA	C22H32O3	M-H	7.58
15(s)-HEPE	C20H30O3	M-H	7.10
15(S)-HETE	C20H32O3	M-H	7.26
15-HETE-d8	C20H24D8O3	M-H	7.26
17(S)-HDHA	C22H32O3	M-H	7.32
18-HEPE	C20H30O3	M-H	6.83
5(S)-HEPE	C20H30O3	M-H	7.33
5(S)-HETE	C20H32O3	M-H	7.85
6-keto_Prostaglandin_F1	C20H34O6	M-H	6.15
8-HEPE	C20H30O3	M-H	7.06
9-HEPE	C20H30O3	M-H	7.13
DHA	C22H32O2	M-H	9.12
DHA-d5	C22H27O2D5	M-H	9.12
DPA3	C22H34O2	M-H	9.41
EPA	C20H30O2	M-H	8.74
EPA-d5	C20H25D5O2	M-H	8.74
Mr1	C22H32O4	M-H	6.22
Mr2	C22H32O4	M-H	6.24
PrD1	C22H32O4	M-H	6.24
Prostaglandin E3	C20H30O5	M-H	4.36
Prostaglandin F3a	C20H30O5	M-H	4.36
Prostaglandin_D2	C20H32O5	M-H	4.87
Prostaglandin_E2	C20H32O5	M-H	4.78
Prostaglandin_F2a	C20H34O5	M-H	5.03
RvD1	C22H32O5	M-H	4.75
RvD2	C22H32O5	M-H	4.97
RvD3	C22H32O5	M-H	4.87
RvD4	C22H32O5	M-H	5.62
RvD5	C22H32O4	M-H	6.15
RvD6	C22H32O4	M-H	6.51
RvE1	C20H30O5	M-H	3.46

RvE2	C20H30O4	M-H	5.65
Thromboxane_B2	C20H34O6	M-H	4.51

Table S2: Serum triglycerides at various time points during treatment.

Time (h)	LMF	STD	ENT
0	2.14 ± 0.73	2.16 ± 0.68	1.27 ± 0.21
3	1.98 ± 0.50	2.24 ± 0.57	1.51 ± 0.24
6	2.34 ± 0.40	2.34 ± 0.53	1.78 ± 0.30
12	2.53 ± 0.67	2.58 ± 0.70	2.38 ± 0.49*
24	1.81 ± 0.52	2.09 ± 0.69	1.45 ± 0.33
48	1.49 ± 0.40*	2.99 ± 1.20*	1.35 ± 0.32
72	1.41 ± 0.24*	1.54 ± 0.38	1.44 ± 0.34
96	1.45 ± 0.29*	1.81 ± 0.46	1.24 ± 0.24
120	1.84 ± 0.61*	1.40 ± 0.37	1.38 ± 0.45

2-way ANOVA Repeated Measures using Time 0 as Control with Dunnet multiple comparison correction. \* denotes  $p < 0.05$ .

Table S3: Blood HDL at various time points during treatment.

Time (h)	LMF	STD	ENT
0	3.80 ± 0.41	4.31 ± 0.61	4.10 ± 0.52
3	3.65 ± 0.34	4.38 ± 0.67	4.03 ± 0.57
6	3.78 ± 0.38	4.28 ± 0.69	4.28 ± 0.61
12	3.89 ± 0.47	4.04 ± 0.64	4.04 ± 0.68
24	3.88 ± 0.41	4.23 ± 0.68	4.32 ± 0.60
48	3.73 ± 0.40	4.19 ± 0.83	4.31 ± 0.56
72	3.78 ± 0.38	4.12 ± 0.66	4.10 ± 0.51
96	3.44 ± 0.39	4.09 ± 0.66	3.79 ± 0.42
120	3.63 ± 0.54	4.18 ± 0.66	4.17 ± 0.53

2-way ANOVA Repeated Measures using Time 0 as Control with Dunnet multiple comparison correction. No significance was found.

Table S4: Blood LDL at various time points during treatment.

Time (h)	LMF	STD	ENT
0	2.90 ± 0.4	3.31 ± 0.49	3.52 ± 0.47
3	2.78 ± 0.35	3.36 ± 0.49	3.34 ± 0.50
6	2.77 ± 0.36	3.21 ± 0.52	3.46 ± 0.52
12	2.81 ± 0.49	2.64 ± 0.40	3.09 ± 0.49
24	3.13 ± 0.47	3.28 ± 0.46	3.65 ± 0.49
48	3.05 ± 0.36	3.32 ± 0.65	3.69 ± 0.47
72	3.14 ± 0.37	3.94 ± 0.33	3.44 ± 0.39

96	$2.78 \pm 0.36$	$3.26 \pm 0.49$	$3.22 \pm 0.34$
120	$2.79 \pm 0.49$	$4.04 \pm 0.42$	$3.54 \pm 0.41$

2-way ANOVA Repeated Measures using Time 0 as Control with Dunnet multiple comparison correction. No significance was found.

Table S5: Blood LDL/HDL Ratio at various time points during treatment.

Time (h)	LMF	STD	ENT
0	$2.03 \pm 0.32$	$2.72 \pm 0.54$	$2.23 \pm 0.50$
3	$2.02 \pm 0.29$	$2.94 \pm 0.65$	$2.13 \pm 0.45$
6	$2.24 \pm 0.34$	$3.08 \pm 0.79$	$2.51 \pm 0.54$
12	$2.10 \pm 0.39$	$2.43 \pm 0.59$	$2.35 \pm 0.57$
24	$2.27 \pm 0.33$	$3.04 \pm 0.64$	$2.33 \pm 0.44$
48	$2.59 \pm 0.41$	$2.93 \pm 0.79$	$2.36 \pm 0.44$
72	$2.46 \pm 0.30$	$3.58 \pm 0.23$	$2.27 \pm 0.40$
96	$2.28 \pm 0.40$	$2.78 \pm 0.55$	$2.21 \pm 0.42$
120	$2.54 \pm 0.61$	$3.95 \pm 0.32$	$2.65 \pm 0.40$

2-way ANOVA Repeated Measures using Time 0 as Control with Dunnet multiple comparison correction. No significance was found.

Table S6: Blood TC at various time points during treatment.

Time (h)	LMF	STD	ENT
0	$5.2 \pm 0.36$	$5.7 \pm 0.38$	$5.88 \pm 0.43$
3	$5.02 \pm 0.35$	$5.73 \pm 0.47$	$5.79 \pm 0.5$
6	$5.03 \pm 0.39$	$5.54 \pm 0.47$	$5.87 \pm 0.53$
12	$5.2 \pm 0.42$	$5.23 \pm 0.46$	$5.34 \pm 0.52$
24	$5.26 \pm 0.42$	$5.5 \pm 0.5$	$6.03 \pm 0.52$
48	$5.03 \pm 0.35$	$5.81 \pm 0.52$	$6.03 \pm 0.49$
72	$5.15 \pm 0.4$	$5.42 \pm 0.51$	$5.77 \pm 0.48$
96	$4.77 \pm 0.34$	$5.44 \pm 0.5$	$5.43 \pm 0.33$
120	$4.92 \pm 0.38$	$5.43 \pm 0.49$	$5.59 \pm 0.55$

2-way ANOVA Repeated Measures using Time 0 as Control with Dunnet multiple comparison correction. No significance was found.

Table S7: Blood non-HDL cholesterol at various time points during treatment.

Time (h)	LMF	STD	ENT
0	$3.8 \pm 0.41$	$4.31 \pm 0.61$	$4.1 \pm 0.52$
3	$3.65 \pm 0.34$	$4.38 \pm 0.67$	$4.03 \pm 0.57$
6	$3.78 \pm 0.38$	$4.28 \pm 0.69$	$4.28 \pm 0.61$
12	$3.89 \pm 0.47$	$4.04 \pm 0.64$	$4.04 \pm 0.68$
24	$3.88 \pm 0.41$	$4.23 \pm 0.68$	$4.32 \pm 0.6$
48	$3.73 \pm 0.4$	$4.19 \pm 0.83$	$4.31 \pm 0.56$
72	$3.78 \pm 0.38$	$4.12 \pm 0.66$	$4.1 \pm 0.51$

96	$3.44 \pm 0.39$	$4.09 \pm 0.66$	$3.79 \pm 0.42$
120	$3.63 \pm 0.54$	$4.18 \pm 0.66$	$4.17 \pm 0.53$

2-way ANOVA Repeated Measures using Time 0 as Control with Dunnet multiple comparison correction. No significance was found.

Table S8: Serum lipid parameters combining all treatments.

Time (h)	HDL	LDL	LDL/HDL	TC	TRG	non-HDL
0	$1.55 \pm 0.11$	$3.27 \pm 0.26$	$2.29 \pm 0.27$	$5.60 \pm 0.23$	$1.80 \pm 0.32$	$4.05 \pm 0.28$
3	$1.52 \pm 0.11$	$3.17 \pm 0.26$	$2.31 \pm 0.27$	$5.50 \pm 0.26$	$1.86 \pm 0.24$	$3.98 \pm 0.3$
6	$1.38 \pm 0.10^*$	$3.14 \pm 0.27$	$2.56 \pm 0.31$	$5.45 \pm 0.27$	$2.14 \pm 0.23$	$4.08 \pm 0.3$
12	$1.34 \pm 0.10^*$	$2.88 \pm 0.26^*$	$2.29 \pm 0.29$	$5.26 \pm 0.26$	$2.49 \pm 0.33^*$	$3.98 \pm 0.32$
24	$1.47 \pm 0.10^*$	$3.36 \pm 0.27$	$2.49 \pm 0.26$	$5.59 \pm 0.27$	$1.75 \pm 0.28$	$4.12 \pm 0.3$
48	$1.48 \pm 0.11$	$3.36 \pm 0.26$	$2.57 \pm 0.28$	$5.60 \pm 0.27$	$1.83 \pm 0.38$	$4.06 \pm 0.31$
72	$1.46 \pm 0.10$	$3.42 \pm 0.22$	$2.63 \pm 0.22$	$5.43 \pm 0.26$	$1.45 \pm 0.17$	$3.98 \pm 0.27$
96	$1.46 \pm 0.11$	$3.09 \pm 0.22$	$2.39 \pm 0.25$	$5.21 \pm 0.22^*$	$1.47 \pm 0.18$	$3.76 \pm 0.27$
120	$1.33 \pm 0.12^*$	$3.42 \pm 0.27$	$2.96 \pm 0.30^*$	$5.33 \pm 0.27$	$1.53 \pm 0.27$	$4.00 \pm 0.31$

2-way ANOVA Repeated Measures using Time 0 as Control with Dunnet multiple comparison correction. \* denotes  $p < 0.05$ .