

Electronic Supplementary Material

Lipidomic profiling of targeted oxylipins with ultra-performance liquid chromatography-tandem mass spectrometry

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Table S1. Evaluation of container transfer losses of analytes

Compound	recovery (0.1 ng/mL)	RDS%	recovery (0.2 ng/mL)*	RDS%	recovery (1 ng/mL)	RDS%
9-HODE	NQ	NA	98.6	3.3	96.3	4.2
13-HODE	NQ	NA	97.3	6.7	98.3	8.2
9-oxoODE	90.3	9.4	106.3	14.7	93.9	6.0
13-oxoODE	102.9	16.3	93.0	5.7	91.5	4.5
9,10-EpOME	97.9	20.8	102.0	6.5	101.2	5.9
12,13-EPOME	NQ	NA	102.2	8.8	102.9	11.8
9,10-DiHOME	101.1	17.3	101.6	3.4	98.2	6.5
12,13-DiHOME	NQ	NA	99.8	4.9	109.3	10.4
9,12,13-TriHOME	NQ	NA	106.3	19.9	114.6	11.4
9,10,13-TriHOME	NQ	NA	109.4	13.7	91.1	16.8
9,10,11-TriHOME	106.2	21.3	115.3	10.2	96.9	8.8
9-HOTrE	85.8	6.6	96.3	2.7	90.5	2.4
13-HOTrE	92.6	8.1	106.4	6.4	89.6	5.9
PGE ₂	97.4	4.5	100.8	4.2	85.3	4.8
PGF _{2α}	NQ	NA	89.0	10.2	106.9	8.6
8-IsoPGF _{2α}	NQ	NA	105.8	5.9	95.4	3.6
TXB ₂	87.4	2.7	95.6	4.4	103.4	5.3
LTB ₄	95.3	9.9	90.7	2.9	95.2	5.3
LXA ₄	86.9	17.5	97.8	4.0	97.3	1.7
LXB ₄	NQ	NA	103.2	7.4	87.5	8.6
5-HETE	86.9	7.1	87.0	6.2	95.7	8.3
8-HETE	84.6	3.6	95.8	5.1	98.6	11.0
9-HETE	83.5	9.0	92.5	10.1	91.7	12.1
11-HETE	86.9	10.6	93.4	3.7	95.5	3.8
12-HETE	NQ	NA	89.3	8.0	85.4	6.6
15-HETE	107.6	18.5	96.5	3.6	87.4	8.8
20-HETE	NQ	NA	112.7	5.0	119.0	14.5
5-oxoETE	86.5	5.9	85.4	5.4	90.6	12.5
5,6-EET	-	-	-	-	53.5	6.6
8,9-EET	80.7	4.4	89.3	4.0	90.9	12.9
11,12-EET	79.8	5.7	82.1	12.1	92.2	2.9
14,15-EET	73.7	12.5	92.2	2.4	103.9	11.4
18-HEPE	84.9	6.8	98.0	3.5	100.8	10.0
14,15-EEQ	80.8	8.5	93.9	2.8	90.8	8.5
17,18-EEQ	90.5	19.1	103.4	7.9	98.0	2.4
4-HDHA	68.9	9.8	84.7	13.3	103.6	8.7
7-HDHA	81.4	9.7	101.2	10.4	108.8	5.3

10-HDHA	73.8	5.8	88.2	8.6	96.8	8.0
14-HDHA	86.4	17.0	106.2	9.9	98.2	10.4
17-HDHA	NQ	NA	93.2	14.3	92.3	7.1
PDX	90.7	4.0	97.9	5.9	96.5	11.3
MaR ₁	93.4	11.6	89.7	4.9	103.3	10.1
RvD ₁	93.2	13.8	92.0	3.2	108.0	4.8
RvD ₂	NQ	NA	100.2	6.4	108.8	5.8
16,17-EDP	69.6	9.2	86.1	5.9	81.2	8.6
19,20-EDP	81.5	5.9	91.4	9.5	85.4	11.5
11-H-9-E-LA 1	NQ	NA	114.6	9.4	113.2	7.1
11-H-9-E-LA 2	NQ	NA	104.6	12.3	94.7	9.5
13-H-9-E-LA	NQ	NA	103.7	12.5	92.4	6.3
9-H-12-E-LA	NQ	NA	110.7	6.3	95.8	10.4
11-H-12-E-LA 1	NQ	NA	96.0	6.8	101.5	14.4
11-H-12-E-LA 2	NQ	NA	70.5	7.6	87.8	23.2

RSD: relative standard deviation. The experiments to check for analyte loss during container transfer were performed in the PMC matrix at concentration levels of 0.1 and 0.2 ng/mL and 1 ng/mL (n=4). *: for RvD₂, 11-H-9-E LAs, and 11-H-12-E LAs, concentration was 0.5 ng/mL. The peak area ratios of pre-spiked samples at these concentrations were compared with those of the spiked samples after the extraction procedure. NQ: the concentration is below the LOQ or out of the linear range or not detected, NA: not available, -: compound not included.

Table S2. Sensitivity and linearity of the method

Compound	LOD (ng/mL)	LOQ (ng/mL)	LLOQ (ng/mL)	R	Linear range (ng/mL)
9-HODE	0.02	0.2	0.2	0.9934	0.2-500
13-HODE	0.02	0.2	0.5	0.9967	0.2-100
9-oxoODE	0.02	0.1	0.2	0.9987	0.1-100
13-oxoODE	0.02	0.1	0.5	0.9979	0.1-100
9,10-EpOME	0.02	0.2	1.0	0.9975	0.2-100
12,13-EPOME	0.02	0.2	1.0	0.9977	0.2-100
9,10-DiHOME	0.02	0.1	0.2	0.9979	0.1-100
12,13-DiHOME	0.02	0.2	0.2	0.9982	0.2-100
9,12,13-TriHOME	0.02	0.2	1.0	0.9977	0.2-100
9,10,13-TriHOME	0.05	0.2	1.0	0.9985	0.2-100
9,10,11-TriHOME	0.05	0.1	0.2	0.9980	0.1-100
9-HOTrE	0.02	0.05	0.1	0.9908	0.05-100
13-HOTrE	0.05	0.1	0.2	0.9991	0.1-100
PGE ₂	0.05	0.1	0.1	0.9986	0.1-100
PGF _{2α}	0.1	0.2	0.5	0.9969	0.2-100
8-IsoPGF _{2α}	0.1	0.2	0.5	0.9994	0.2-100
TXB ₂	0.05	0.1	0.2	0.9993	0.1-100
LTB ₄	0.02	0.05	0.1	0.9992	0.05-100
LXA ₄	0.05	0.1	0.2	0.9990	0.1-100
LXB ₄	0.10	0.2	0.5	0.9988	0.2-100
5-HETE	0.02	0.1	0.1	0.9976	0.1-100
8-HETE	0.05	0.1	0.2	0.9978	0.1-100
9-HETE	0.05	0.2	0.2	0.9976	0.2-100
11-HETE	0.02	0.1	0.1	0.9986	0.1-100
12-HETE	0.05	0.2	0.2	0.9986	0.2-100
15-HETE	0.05	0.1	0.2	0.9990	0.1-100
20-HETE	0.1	0.2	0.2	0.9944	0.2-100
5-oxoETE	0.02	0.1	0.2	0.9977	0.1-100
5,6-EET	0.1	0.2	0.5	0.9990	0.2-100
8,9-EET	0.02	0.1	0.1	0.9990	0.1-100
11,12-EET	0.02	0.1	0.1	0.9985	0.1-100
14,15-EET	0.02	0.1	0.1	0.9989	0.1-100
18-HEPE	0.02	0.1	0.1	0.9992	0.1-100
14,15-EEQ	0.02	0.1	0.1	0.9984	0.1-100
17,18-EEQ	0.02	0.1	0.2	0.9975	0.1-100
4-HDHA	0.05	0.1	0.2	0.9989	0.1-100
7-HDHA	0.05	0.1	0.2	0.9991	0.1-100
10-HDHA	0.05	0.1	0.2	0.9991	0.1-100
14-HDHA	0.05	0.1	0.2	0.9984	0.2-100
17-HDHA	0.1	0.2	0.5	0.9991	0.2-100

PDX	0.02	0.05	0.1	0.9992	0.05-100
MaR ₁	0.05	0.1	0.1	0.9994	0.1-100
RvD ₁	0.05	0.1	0.1	0.9992	0.1-100
RvD ₂	0.1	0.2	0.5	0.9994	0.5-100
16,17-EDP	0.05	0.1	0.2	0.9984	0.1-100
19,20-EDP	0.05	0.1	0.2	0.9985	0.1-100
11-H-9-E-LA	0.10	0.5	0.5	0.9996	0.5-100
13-H-9-E-LA	0.10	0.2	0.5	0.9985	0.2-100
9-H-12-E-LA	0.10	0.2	0.2	0.9990	0.2-100
11-H-12-E-LA	0.20	0.5	1.0	0.9992	0.5-100

Limit of detection (LOD), limit of quantitation (LOQ), lower limit of quantitation (LLOQ), RSD: relative standard deviation, R: correlation coefficient. The LODs, LOQs, and LLOQs were determined from a series of diluted calibration standard solutions following SPE. The LODs were defined as the concentration that had S/N >3, and LOQs were the lowest value on the standard curve for each analyte with S/N > 5 and resulted in RSDs < 25% (n = 4). The LLOQs were defined to be concentrations at which the analyte peaks are reproducible with RSD of <20% and accuracy of 70-130%. NQ: the concentration is below the LLOQ or out of the linear range or not detected, NA: not available, -: compound not included.

Table S3. Autosampler stability of analytes in reconstitution solution from PMC and plasma extract

Compound	% Remaining after 24 h											
	QC3 (1 ng/mL)*				QC4 (10 ng/mL)*				QC5 (80 ng/mL)*			
	PMC		Plasma		PMC		Plasma		PMC		Plasma	
	Stability	RSD%	Stability	RSD%	Stability	RSD%	Stability	RSD%	Stability	RSD%	Stability	RSD%
9-HODE	99.0	1.0	102.0	1.8	102.6	3.2	101.9	2.5	104.7	2.2	104.1	2.0
13-HODE	108.9	5.4	98.5	1.3	102.4	2.5	100.2	2.0	102.6	1.6	104.5	2.9
9-oxoODE	96.5	6.4	101.1	9.1	99.0	4.0	97.4	3.6	97.3	2.9	98.3	0.4
13-oxoODE	104.9	6.1	102.3	5.5	101.2	1.9	99.4	4.3	100.6	1.3	100.8	1.9
9,10-EpOME	105.2	6.1	104.0	2.1	101.8	0.9	102.5	1.6	103.2	3.6	103.0	3.3
12,13-EPOME	108.2	8.2	101.2	3.1	99.0	2.9	101.4	1.5	101.4	3.6	100.7	1.9
9,10-DiHOME	99.0	3.2	98.5	2.6	98.6	2.6	98.5	2.5	102.9	3.3	99.2	1.6
12,13-DiHOME	100.6	1.9	94.9	4.2	100.3	2.6	97.5	2.7	102.1	1.7	96.7	2.4
9,12,13-TriHOME	93.6	3.4	100.3	2.2	98.1	2.4	103.7	3.3	105.8	4.9	103.5	2.1
9,10,13-TriHOME	91.7	6.3	99.1	3.2	96.4	3.3	102.8	3.3	102.4	2.9	102.7	1.6
9,10,11-TriHOME	98.4	2.1	100.6	5.5	100.2	1.6	99.8	4.8	101.4	2.6	104.6	3.4
9-HOTrE	103.9	1.8	102.4	2.5	104.2	3.4	103.5	2.5	106.4	3.1	104.2	2.3
13-HOTrE	104.0	3.4	101.7	4.5	104.9	4.4	101.2	2.9	101.9	2.4	102.4	2.4
PGE ₂	94.8	3.0	111.4	12.9	98.2	2.3	92.3	14.7	98.1	3.6	112.0	9.7
PGF _{2α}	89.3	5.4	95.6	3.6	102.7	4.2	104.1	5.2	106.9	3.2	105.4	1.6
8-IsoPGF _{2α}	100.4	10.8	92.3	4.6	103.8	5.9	102.5	3.6	102.7	1.8	104.6	2.2
TXB ₂	99.3	5.5	102.3	3.6	104.1	9.1	103.8	5.0	104.9	2.2	102.2	3.2
LTB ₄	100.3	3.8	101.3	4.9	103.6	3.1	100.1	2.8	103.1	3.0	100.4	0.5
LXA ₄	100.1	7.1	99.5	9.8	100.8	0.6	100.9	4.2	102.4	2.9	100.9	2.5
LXB ₄	102.2	7.9	99.3	9.1	101.2	2.4	102.7	6.7	101.2	1.5	101.9	2.2
5-HETE	97.9	7.3	100.9	2.9	97.8	2.5	99.9	2.4	98.6	1.6	100.9	2.2
8-HETE	91.5	7.8	100.9	3.4	97.9	2.9	99.3	3.3	97.7	1.5	104.8	5.3
9-HETE	103.2	7.5	106.5	7.2	100.0	7.0	102.4	4.1	97.3	1.8	100.9	1.4
11-HETE	95.3	3.5	99.9	5.7	98.1	3.1	97.2	4.1	97.8	1.9	98.7	2.2
12-HETE	104.7	14.5	100.9	8.3	102.6	7.4	96.5	3.5	100.1	1.3	98.7	3.0
15-HETE	103.6	5.9	98.3	9.3	100.9	4.5	104.4	4.1	99.9	4.0	110.2	2.5
20-HETE	104.4	11.1	96.8	7.0	104.0	3.6	105.6	5.9	100.6	2.7	108.5	6.8
5-oxoETE	104.4	6.5	95.4	1.9	101.5	2.5	97.1	6.1	100.7	4.4	93.3	6.9

5,6-EET	109.2	9.9	103.9	11.4	100.5	12.1	98.2	6.1	102.1	3.5	99.6	12.1
8,9-EET	103.3	1.3	98.4	3.6	99.2	1.6	100.3	2.1	100.2	3.9	97.5	3.5
11,12-EET	99.7	4.2	96.6	1.8	99.3	1.5	99.1	3.8	101.5	4.5	96.7	4.1
14,15-EET	103.1	5.8	98.2	3.9	99.1	0.3	101.4	2.4	100.5	3.4	99.7	1.5
18-HEPE	101.1	5.8	103.9	3.8	105.8	3.7	99.3	1.4	101.0	2.4	100.4	1.9
14,15-EEQ	95.5	6.9	102.9	8.4	101.0	1.9	103.7	2.4	100.7	1.5	103.0	2.5
17,18-EEQ	98.7	12.4	105.7	6.3	97.5	4.3	98.8	2.5	96.8	1.7	100.9	2.1
4-HDHA	96.4	6.9	105.3	7.4	100.5	1.8	99.5	2.3	99.0	1.0	104.8	3.6
7-HDHA	100.9	7.2	101.8	4.1	101.7	1.3	100.6	1.7	101.4	2.4	102.1	1.3
10-HDHA	95.7	6.1	96.8	6.4	99.7	1.5	98.2	2.9	100.0	1.0	99.7	1.1
14-HDHA	103.4	14.4	101.5	13.0	99.0	4.5	93.3	5.1	103.7	4.3	96.0	3.2
17-HDHA	110.9	13.1	101.4	8.5	96.7	2.6	97.6	2.6	98.4	6.2	95.5	2.6
PDX	101.2	3.7	97.0	3.9	105.1	2.1	98.4	2.1	105.5	1.1	101.0	0.9
MaR ₁	100.3	8.8	94.8	7.9	103.1	3.1	98.8	1.7	107.5	1.9	100.6	2.5
RvD ₁	100.2	7.4	98.7	6.1	96.4	2.7	103.0	4.3	99.6	1.6	100.5	0.9
RvD ₂	91.5	10.3	104.1	5.7	99.1	1.7	103.2	2.5	102.1	0.3	103.0	2.4
16,17-EDP	108.5	5.8	103.7	3.4	100.5	2.1	99.5	1.2	101.1	3.4	100.4	1.9
19,20-EDP	103.5	11.6	100.7	4.6	99.5	2.2	100.8	4.5	103.0	2.5	99.2	4.0
11-H-9-E-LA	105.9	11.4	98.0	13.6	102.0	6.0	99.9	6.0	101.3	3.5	99.5	2.8
13-H-9-E-LA	105.6	11.0	102.6	7.7	100.2	3.5	100.8	5.8	102.7	2.5	98.4	5.8
9-H-12-E-LA	100.2	11.2	97.7	4.3	100.3	2.4	101.3	3.3	101.3	1.3	100.2	2.0
11-H-12-E-LA	109.2	6.1	113.4	9.1	102.5	3.3	102.2	4.5	103.1	2.1	99.1	2.2

*: for 9-HODE and 9-HOTrE, concentration levels of QC3, QC4, and QC5 were 10, 100, and 800, respectively. RSD: relative standard deviation. Stability of analytes was determined by injecting processed QC samples (n=4) on three levels (QC3, QC4, and QC5) from PMC or pooled plasma. The extracts were stored in the autosampler at 4 °C and injected at T=0 h and T=24 h. Relative MS signals between the two time points were compared as percent of T=0 h.

Table S4. Intraday and interday accuracy and precision (n=4) for quality control samples at four different concentration levels from PMC extracts

Compound	QC1 (0.2 ng/mL)*				QC 3 (1 ng/mL)*				QC 4 (10 ng/mL)*				QC 5 (80 ng/mL)*			
	Intra-day		Inter-day		Intra-day		Inter-day		Intra-day		Inter-day		Intra-day		Inter-day	
	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%
9-HODE	104.3	3.7	94.9	9.4	85.9	5.0	102.8	12.9	93.3	1.9	115.8	14.6	NQ	NA	NQ	NA
13-HODE	NQ	NA	NQ	NA	83.7	7.2	95.3	11.6	80.7	1.4	92.4	11.8	113.5	6.1	115.2	8.5
9-oxoODE	116.2	3.5	101.6	16.9	87.8	6.2	98.2	11.7	89.2	2.4	93.4	7.1	110.8	6.7	110.1	6.3
13-oxoODE	110.1	13.3	110.0	27.7	75.9	2.3	91.6	14.7	82.7	1.7	92.3	9.8	109.5	6.0	112.5	5.8
9,10-EpOME	NQ	NA	NQ	NA	82.6	1.8	90.3	7.8	87.6	3.6	93.6	7.3	104.5	3.4	106.0	4.5
12,13-EPOME	NQ	NA	NQ	NA	69.3	9.8	85.7	16.7	91.7	0.4	95.8	6.2	106.8	4.9	105.7	4.3
9,10-DiHOME	116.9	5.3	110.3	6.7	84.9	3.9	96.2	10.2	87.8	0.9	100.6	12.1	105.4	4.7	111.4	8.5
12,13-DiHOME	118.0	3.5	121.0	6.9	84.0	7.0	98.9	12.1	82.7	2.3	95.8	11.8	109.3	6.5	113.3	9.3
9,12,13-TriHOME	NQ	NA	NQ	NA	78.1	5.6	98.8	21.7	86.9	4.5	94.2	11.8	114.8	4.2	113.8	8.4
9,10,13-TriHOME	NQ	NA	NQ	NA	88.5	10.3	104.2	14.8	92.3	3.9	99.8	12.0	109.0	4.7	110.8	8.4
9,10,11-TriHOME	104.1	10.7	95.3	12.9	90.3	4.9	101.3	10.0	91.3	3.0	90.7	10.4	116.0	7.0	113.6	8.1
9-HOTrE	101.8	2.7	96.5	4.5	92.2	2.7	110.1	13.9	97.9	1.8	119.5	17.8	NQ	NA	NQ	NA
13-HOTrE	111.0	7.4	97.7	12.5	89.1	6.1	102.9	11.3	85.3	3.2	113.2	17.5	107.5	5.8	111.4	10.7
PGE ₂	113.9	7.9	102.9	12.2	96.0	5.8	101.1	7.8	88.2	5.4	100.4	10.3	99.6	7.2	106.4	9.3
PGF _{2α}	NQ	NA	NQ	NA	89.8	6.8	102.8	10.1	93.9	2.0	93.8	9.6	115.5	4.9	112.9	8.6
8-IsoPGF _{2α}	NQ	NA	NQ	NA	88.2	9.2	105.0	14.0	110.3	5.0	101.4	9.8	125.8	4.7	113.9	10.9
TXB ₂	104.3	4.7	103.8	10.3	93.8	3.2	100.0	9.5	92.7	4.0	103.1	12.8	107.4	9.3	107.8	9.5
LTB ₄	104.4	3.1	93.8	10.5	97.1	3.6	101.7	7.2	94.1	3.5	99.9	7.4	109.8	5.8	108.0	6.8
LXA ₄	100.8	3.9	102.1	6.2	96.3	6.9	106.0	9.2	93.8	3.4	97.3	10.0	111.0	6.1	108.7	8.8
LXB ₄	NQ	NA	NQ	NA	84.3	7.0	99.2	17.9	103.0	1.8	103.9	10.5	111.8	4.2	110.0	8.9
5-HETE	97.1	6.4	95.3	5.9	91.5	0.9	99.0	8.5	86.9	5.4	96.6	9.8	109.5	6.5	110.9	7.0
8-HETE	103.6	4.6	98.9	10.5	86.8	3.8	94.2	6.8	81.3	3.6	90.8	11.0	109.7	7.8	110.8	8.4
9-HETE	99.5	9.7	96.1	8.9	92.9	1.9	95.9	6.4	83.4	9.8	94.6	11.7	103.5	8.8	106.8	6.5
11-HETE	101.9	3.2	106.5	10.3	84.9	3.1	96.1	9.2	81.7	4.2	90.7	10.9	110.0	7.4	111.8	9.2
12-HETE	108.1	7.5	95.9	15.0	91.5	10.0	100.1	12.8	97.6	2.9	96.6	6.6	112.5	6.9	109.8	7.6
15-HETE	113.5	4.6	106.1	14.4	91.3	4.3	105.1	12.2	87.1	2.7	96.2	9.8	111.0	8.1	111.2	9.5
20-HETE	105.5	6.3	101.3	12.5	102.7	10.2	102.2	7.9	89.4	7.1	99.3	7.5	102.1	7.5	106.7	6.8
5-oxoETE	98.1	5.6	106.4	10.6	101.4	14.4	102.6	9.7	121.0	8.3	95.6	16.3	125.3	2.7	114.8	9.7
5,6-EET	-	-	-	-	89.3	13.4	97.5	13.8	88.3	3.7	104.3	11.2	96.0	6.9	106.0	10.8

8,9-EET	106.1	4.1	109.5	14.2	91.0	2.2	95.4	6.6	91.0	3.6	92.7	7.1	108.7	6.6	105.9	5.7
11,12-EET	102.1	12.1	105.4	12.3	96.5	6.0	98.7	7.0	89.1	4.9	93.1	7.8	108.4	6.1	105.5	5.2
14,15-EET	101.0	2.5	104.7	5.6	86.8	3.2	96.5	8.5	85.6	3.9	93.3	8.8	109.8	5.4	111.8	5.3
18-HEPE	104.9	3.5	95.4	9.6	93.3	5.7	107.7	13.0	101.5	0.6	111.9	11.5	102.2	6.8	108.6	10.7
14,15-EEQ	103.6	3.0	105.5	8.5	91.8	3.7	97.8	6.7	95.3	2.0	94.7	7.1	105.6	6.2	106.4	5.1
17,18-EEQ	98.3	8.6	102.2	11.8	100.7	9.3	106.0	7.6	90.6	4.5	93.6	8.1	106.8	4.7	108.5	5.8
4-HDHA	111.0	10.2	94.5	17.1	94.6	4.8	96.4	6.4	85.2	3.3	92.0	9.3	112.5	8.5	112.7	7.2
7-HDHA	114.1	10.4	117.3	11.6	98.1	5.4	105.4	7.2	92.7	4.6	102.0	11.0	108.5	6.7	109.9	8.6
10-HDHA	96.5	8.5	99.3	8.3	92.9	5.0	99.2	7.1	89.1	3.3	98.6	10.8	106.2	7.5	108.9	9.9
14-HDHA	111.1	8.5	105.5	13.3	92.6	6.6	98.6	7.1	89.7	6.8	95.8	8.8	110.5	7.5	111.4	8.5
17-HDHA	NQ	NA	NQ	NA	105.8	8.5	101.6	8.6	94.3	3.0	101.5	12.1	109.8	7.1	109.4	9.2
PDX	96.5	6.1	102.3	6.8	95.0	0.7	102.1	8.5	90.3	2.9	100.6	9.7	117.8	6.8	116.1	8.2
MaR ₁	100.9	5.2	101.0	10.2	94.2	9.4	101.3	8.8	93.3	2.0	99.9	9.3	108.0	6.3	107.7	7.2
RvD ₁	96.3	3.1	97.2	10.8	99.5	11.8	103.5	11.6	103.5	2.0	106.7	9.5	106.9	6.6	108.3	7.0
RvD ₂	NQ	NA	NQ	NA	93.6	11.0	101.9	12.6	100.8	6.3	102.6	10.5	106.6	6.1	107.4	6.3
16,17-EDP	109.4	6.1	113.8	13.9	88.1	5.6	94.3	7.2	90.6	4.7	92.2	8.9	108.3	5.9	105.4	5.2
19,20-EDP	105.3	9.2	104.0	9.2	89.8	2.9	97.1	8.8	97.3	4.4	97.6	8.7	107.5	5.9	104.7	5.2
11-H-9-E-LA	NQ	NA	NQ	NA	129.6	4.1	143.1	11.0	96.0	1.7	100.4	9.3	106.9	6.6	108.4	8.7
13-H-9-E-LA	122.9	10.8	118.5	25.4	109.0	5.9	94.5	24.3	84.1	0.6	91.1	8.0	113.8	7.4	112.8	6.1
9-H-12-E-LA	127.1	6.6	117.8	22.9	77.0	15.3	94.0	16.0	88.9	2.9	95.0	7.6	109.5	6.4	110.6	5.3
11-H-12-E-LA	NQ	NA	NQ	NA	114.9	6.6	139.6	23.1	96.0	6.7	100.1	9.5	108.8	7.5	109.6	7.9

*: for 9-HODE and 9-HOTrE, concentration levels of QC1, QC3, QC4, and QC5 were 2, 10, 100, and 800, respectively. AC: accuracy, RSD: relative standard deviation. Accuracy is displayed as the mean of the assayed concentration in percent of the spiked concentration (n=4). Precision is displayed as the relative standard deviation (RSD) of the intraday and interday replicate analysis, and calculated by taking the calculated standard deviation and dividing by the mean of the assayed concentration for each analyte. AC: accuracy, RSD: relative standard deviation, NQ: the concentration is below the LLOQ or out of the linear range or not detected, NA: not available, -: compound not included.

Table S5. Intraday and interday accuracy and precision (n=4) for quality control samples at five different concentration levels from plasma extracts

Compound	QC1 (0.2 ng/mL)*				QC2 (0.5 ng/mL)*				QC3 (1 ng/mL)*				QC4 (10 ng/mL)*				QC5 (80 ng/mL)*			
	Intra-day		Inter-day		Intra-day		Inter-day		Intra-day		Inter-day		Intra-day		Inter-day		Intra-day		Inter-day	
	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%	AC%	RSD%
9-HODE	92.8	10.4	92.6	9.7	95.4	1.7	89.9	10.6	103.6	3.2	107.9	5.2	109.3	2.0	119.2	6.8	NQ	NA	NQ	NA
13-HODE	NQ	NA	NQ	NA	97.5	20.3	109.5	19.2	120.0	16.1	110.0	17.3	88.5	3.0	109.7	14.5	105.9	4.1	113.5	7.2
9-oxoODE	95.0	20.2	92.2	23.3	72.0	6.0	70.7	6.7	82.7	11.7	84.6	9.8	80.0	1.5	92.1	11.1	90.4	6.7	101.6	11.9
13-oxoODE	116.5	12.3	98.8	28.7	70.4	8.3	73.6	9.3	84.6	10.2	81.7	11.9	71.7	1.4	82.6	11.5	84.4	9.1	91.5	11.9
9,10-EpOME	NQ	NA	NQ	NA	NQ	NA	NQ	NA	88.3	10.5	89.1	14.0	75.7	1.5	83.2	9.4	84.0	8.5	85.3	5.9
12,13-EPOME	NQ	NA	NQ	NA	NQ	NA	NQ	NA	98.8	13.5	108.0	19.3	78.2	1.9	83.4	11.6	87.6	8.8	92.9	8.4
9,10-DiHOME	87.8	10.2	77.8	19.6	90.3	5.5	83.7	17.4	101.2	7.8	112.6	9.3	104.6	3.5	120.7	10.3	103.2	2.8	115.0	10.1
12,13-DiHOME	83.7	14.9	88.2	18.1	82.3	11.7	75.4	15.5	82.3	8.4	102.4	16.6	90.8	3.3	109.0	12.6	103.4	1.6	117.2	11.1
9,12,13-TriHOME	NQ	NA	NQ	NA	NQ	NA	NQ	NA	89.5	17.4	98.0	15.3	91.5	4.7	102.3	8.9	98.1	4.2	110.7	10.4
9,10,13-TriHOME	NQ	NA	NQ	NA	NQ	NA	NQ	NA	105.4	9.5	105.0	8.1	94.6	3.9	105.1	7.9	102.1	3.2	113.7	9.4
9,10,11-TriHOME	82.4	1.7	84.3	8.3	77.9	2.9	78.5	3.0	87.4	8.3	92.6	8.8	92.1	1.6	102.8	8.1	105.6	1.5	120.1	10.0
9-HOTrE	73.6	7.2	78.7	10.5	74.9	0.7	72.8	14.3	85.9	3.4	97.3	9.4	93.6	1.9	108.8	10.7	NQ	NA	NQ	NA
13-HOTrE	70.9	12.9	89.7	30.1	95.9	5.1	76.2	19.6	99.8	3.9	110.2	9.5	95.3	3.0	110.6	10.8	98.9	2.4	115.3	11.6
PGE ₂	94.8	5.0	77.0	19.0	83.6	2.4	80.4	14.3	85.5	10.4	92.0	11.5	95.2	6.5	106.9	9.4	96.7	6.0	109.8	12.2
PGF _{2α}	NQ	NA	NQ	NA	NQ	NA	NQ	NA	92.0	8.4	92.0	7.8	90.2	5.9	96.4	6.2	94.3	3.0	106.4	10.1
8-IsoPGF _{2α}	NQ	NA	NQ	NA	73.1	9.0	75.6	9.5	90.0	11.9	99.0	12.8	96.8	3.0	107.3	7.6	101.0	3.2	113.6	13.0
TXB ₂	88.1	9.0	93.0	14.2	88.7	1.6	86.1	4.5	111.0	3.8	108.0	3.9	98.5	1.8	107.9	7.1	102.5	4.2	110.5	9.0
LTB ₄	86.6	15.2	90.4	11.2	76.4	3.0	79.1	5.7	108.3	2.7	107.9	3.6	103.3	2.0	110.1	5.0	108.0	2.5	115.5	7.8
LXA ₄	95.6	12.2	96.2	9.1	87.4	5.5	80.7	7.3	97.2	5.4	98.4	5.3	96.7	4.2	104.1	5.8	102.9	2.8	114.1	9.5
LXB ₄	NQ	NA	NQ	NA	75.0	3.2	77.1	7.3	118.3	8.1	117.8	9.5	107.0	3.8	114.0	5.4	104.2	3.4	116.4	10.7
5-HETE	101.8	7.5	88.1	15.9	73.5	4.6	83.2	12.0	97.4	5.5	102.7	6.4	96.1	1.1	106.5	8.1	107.3	1.5	120.0	10.1
8-HETE	94.3	11.6	93.3	10.7	67.8	3.1	67.9	3.7	75.0	4.4	79.3	7.0	74.2	0.6	84.0	10.7	89.1	7.9	97.8	11.8
9-HETE	86.8	6.7	86.6	10.8	77.4	5.2	77.8	12.9	84.4	2.0	88.6	8.4	78.2	3.4	88.2	10.4	87.8	8.0	97.8	12.8
11-HETE	93.5	10.2	92.6	14.8	72.8	1.7	69.0	5.4	72.5	2.7	79.5	9.3	75.2	1.2	87.0	12.5	89.5	6.6	101.2	13.7
12-HETE	100.0	10.2	104.7	13.2	72.4	6.7	72.9	9.7	80.6	7.4	91.4	12.0	91.8	4.4	99.0	7.8	99.0	5.3	106.8	9.8
15-HETE	101.3	12.5	124.4	20.4	87.7	10.5	82.4	8.6	92.6	8.0	104.1	10.2	94.2	4.1	108.5	10.9	101.0	4.7	118.5	14.4
20-HETE	110.9	11.3	103.3	18.9	85.8	5.6	85.1	9.2	96.1	11.5	102.3	13.4	96.4	6.8	105.9	14.3	98.1	7.4	109.3	10.4

5-oxoETE	118.9	9.2	126.0	9.6	103.1	2.2	77.7	24.5	98.1	4.3	103.5	9.5	95.3	2.2	116.2	15.7	109.4	11.9	124.2	11.9
5,6-EET	-	-	-	-	-	-	-	-	107.6	7.2	99.1	14.3	99.7	6.9	122.1	15.7	110.5	3.0	129.3	13.4
8,9-EET	106.9	8.9	100.8	10.4	70.3	4.9	70.2	5.4	108.4	3.5	105.3	13.1	107.1	5.0	116.3	12.5	111.6	2.5	117.6	16.1
11,12-EET	108.2	9.3	102.8	10.5	71.0	6.7	70.9	5.2	107.0	6.1	102.8	13.3	112.0	2.2	115.1	8.2	102.8	3.0	113.6	16.3
14,15-EET	102.5	6.7	96.4	9.5	73.5	2.0	75.1	3.3	104.9	4.8	101.7	6.3	101.9	0.6	107.3	5.0	103.7	3.8	111.3	11.3
18-HEPE	72.3	3.6	89.1	23.8	98.7	3.2	80.3	19.0	114.1	2.6	111.4	6.0	104.1	2.4	112.6	6.9	101.4	3.7	112.7	9.0
14,15-EEQ	118.5	7.1	103.7	17.5	73.4	1.5	68.1	6.4	114.0	6.3	112.3	9.3	108.5	4.8	119.2	9.1	114.0	2.6	123.4	11.0
17,18-EEQ	99.0	6.7	99.4	11.6	75.7	3.5	70.3	6.3	101.3	5.1	97.1	7.8	97.7	1.9	102.7	6.3	104.6	2.9	108.8	10.8
4-HDHA	91.1	8.6	100.3	11.5	88.8	5.0	87.2	6.6	87.4	4.5	92.6	6.5	89.0	2.8	100.4	10.9	101.4	7.2	112.5	10.8
7-HDHA	112.3	9.0	95.1	18.6	80.3	7.1	77.7	6.9	96.3	3.6	97.3	9.9	87.4	3.5	97.9	10.4	91.6	5.4	102.8	12.4
10-HDHA	98.1	15.0	93.1	12.4	73.3	1.4	72.1	4.2	82.2	4.3	88.8	7.9	87.8	2.3	97.7	10.0	95.1	6.3	106.4	11.4
14-HDHA	90.5	9.3	97.8	14.3	81.4	7.5	74.7	9.6	82.0	5.1	86.7	6.7	89.5	5.0	98.8	10.5	101.1	7.1	112.2	11.2
17-HDHA	103.8	12.4	97.0	23.7	73.5	14.3	79.9	13.3	109.3	9.3	107.7	11.0	105.0	3.4	114.8	8.0	102.9	6.1	118.2	12.4
PDX	114.0	6.5	104.5	9.6	90.1	1.7	88.6	3.3	111.3	2.4	112.0	2.5	108.0	0.8	117.3	6.2	111.9	1.6	120.7	7.5
MaR ₁	94.5	14.0	93.9	9.7	88.4	6.9	84.4	6.5	112.8	9.3	110.9	5.8	106.0	2.2	113.5	5.6	109.9	0.9	119.9	8.1
RvD ₁	104.6	12.0	102.8	9.9	81.5	4.5	82.3	4.9	114.3	8.1	117.9	10.0	122.5	2.0	128.5	7.8	120.0	4.1	127.6	7.1
RvD ₂	NQ	NA	NQ	NA	79.7	2.3	80.3	8.0	118.3	5.4	108.9	10.1	104.6	6.2	108.4	5.3	102.3	3.0	109.5	8.9
16,17-EDP	99.7	9.6	101.2	10.4	79.0	2.3	70.5	8.7	102.0	3.7	105.8	4.5	99.9	1.9	112.4	8.8	108.4	3.2	117.0	10.6
19,20-EDP	120.5	10.7	110.2	11.7	79.3	3.6	71.3	9.8	114.7	4.4	113.2	10.4	108.8	2.9	124.6	12.2	114.7	3.3	125.0	15.1
11-H-9-E-LA	NQ	NA	NQ	NA	74.9	9.1	71.9	8.5	100.1	9.5	90.9	15.4	96.1	4.6	109.6	9.5	105.1	1.4	118.0	10.3
13-H-9-E-LA	81.1	14.5	91.7	18.3	76.9	3.8	80.3	12.6	89.9	8.0	91.9	10.4	93.8	0.6	101.9	6.1	110.2	1.9	110.9	3.4
9-H-12-E-LA	93.6	10.1	93.8	10.0	70.4	7.9	73.1	15.1	113.5	10.4	100.4	12.3	108.3	1.6	108.4	4.0	114.5	2.4	112.2	3.8
11-H-12-E-LA	NQ	NA	NQ	NA	NQ	NA	NQ	NA	96.8	14.8	103.9	18.2	81.1	2.2	100.6	15.5	98.8	0.6	118.1	13.0

*: for 9-HODE and 9-HOTrE, concentration levels of QC1, QC2, QC3, QC4, and QC5 were 2, 5, 10, 100, and 800, respectively. AC: accuracy, RSD: relative standard deviation. Accuracy is displayed as the mean of the assayed concentration (corrected by endogenous oxylipin concentrations in human plasma) in percent of the spiked concentration. Each value represents the mean of four determinations. Precision is displayed as the relative standard deviation (RSD) expressed as a percentage of the intraday and interday replicate analysis, and calculated by taking the calculated standard deviation and dividing by the mean of the assayed concentration for each analyte. NQ: the concentration is below the LLOQ or out of the linear range or not detected, NA: not available, -: compound not included.

Table S6. Relative matrix effects of targeted oxylipins by comparing post-spiked QC plasma samples with post-spiked QC PMC samples (n=3 or 4)

Compound	Matrix effect		Matrix effect		Matrix effect	
	QC3 (1 ng/mL)*	RDS%	QC4 (10 ng/mL)*	RDS%	QC5 (80 ng/mL)*	RDS%
9-HODE	127.0	10.9	124.5	11.9	120.4	6.0
13-HODE	98.1	17.9	114.1	14.9	105.5	9.8
9-oxoODE	91.8	14.4	96.1	9.3	101.2	18.9
13-oxoODE	96.6	14.8	91.6	10.7	91.4	18.2
9,10-EpOME	NA	NA	81.7	10.8	83.7	10.3
12,13-EPOME	NA	NA	73.9	13.6	87.8	13.1
9,10-DiHOME	142.2	10.7	144.5	13.7	124.7	9.6
12,13-DiHOME	130.1	15.6	137.3	13.1	124.8	10.6
9,12,13-TriHOME	114.0	17.9	117.2	11.3	108.2	13.5
9,10,13-TriHOME	127.8	9.9	117.7	11.0	109.5	10.7
9,10,11-TriHOME	100.4	10.5	114.6	11.6	109.2	17.0
9-HOTrE	120.8	11.6	116.2	9.7	116.1	6.1
13-HOTrE	128.4	10.7	130.7	13.6	119.8	13.4
PGE ₂	108.7	7.0	129.3	15.2	134.0	9.3
PGF _{2α}	117.2	10.6	104.2	12.3	97.3	15.7
8-IsoPGF _{2α}	118.1	11.7	98.6	10.9	99.0	15.6
TXB ₂	118.4	8.0	118.5	12.2	112.8	14.4
LTB ₄	115.5	9.9	117.3	12.4	116.4	14.1
LXA ₄	115.0	14.8	109.8	10.6	114.0	13.4
LXB ₄	142.6	16.5	108.5	9.8	113.2	15.9
5-HETE	106.9	13.8	110.2	12.0	115.6	16.7
8-HETE	85.2	9.9	87.1	11.5	93.2	19.1
9-HETE	109.2	8.1	93.9	10.4	95.8	13.2
11-HETE	91.3	8.5	92.5	9.4	93.5	15.0
12-HETE	100.7	12.9	92.6	9.2	100.2	16.1
15-HETE	110.8	10.7	111.3	9.0	109.7	17.0
20-HETE	78.0	17.9	96.4	9.6	99.9	21.6
5-oxoETE	91.9	21.9	82.7	11.3	89.3	5.6
5,6-EET	120.7	8.7	97.8	11.1	102.6	11.4
8,9-EET	87.5	9.7	88.3	11.2	92.8	16.2
11,12-EET	81.4	1.4	88.0	10.3	89.8	16.8
14,15-EET	96.0	11.9	115.6	12.5	107.2	13.5
18-HEPE	81.9	8.0	119.4	10.5	130.6	11.4
14,15-EEQ	125.6	11.1	92.2	11.8	102.9	16.0
17,18-EEQ	109.4	8.8	87.4	11.2	93.2	21.4
4-HDHA	87.5	9.4	90.2	10.0	92.1	17.8
7-HDHA	96.2	11.4	86.5	11.9	94.5	18.4

10-HDHA	83.9	11.6	93.6	10.5	102.6	18.1
14-HDHA	82.8	12.4	90.8	10.3	102.7	19.6
17-HDHA	118.8	16.0	100.8	8.5	106.5	15.5
PDX	120.0	9.6	125.4	12.1	112.7	13.1
MaR ₁	139.1	7.0	128.3	13.4	129.5	13.2
RvD ₁	136.5	10.2	129.3	8.0	125.9	8.8
RvD ₂	104.2	17.1	109.9	9.5	113.6	14.1
16,17-EDP	85.1	14.3	81.0	12.7	84.0	16.2
19,20-EDP	87.9	4.9	89.9	12.4	100.8	17.9
11-H-9-E-LA	NA	NA	116.2	14.6	132.1	12.8
13-H-9-E-LA	111.9	12.1	118.3	13.2	113.4	14.5
9-H-12-E-LA	125.6	8.9	123.3	13.7	116.3	14.6
11-H-12-E-LA	NA	NA	141.1	17.2	126.2	12.4

The matrix effect is quantified at three concentration levels (QC3, QC4, and QC5) by calculating the ratio the concentration calculated from post-extraction spiked samples prepared in plasma that corrected with endogenous concentration over the concentration calculated post-extraction spiked samples prepared in PMC. *: for 9-HODE and 9-HOTrE, concentration levels of QC3, QC4, and QC5 were 10, 100, and 800, respectively. NA: not available.

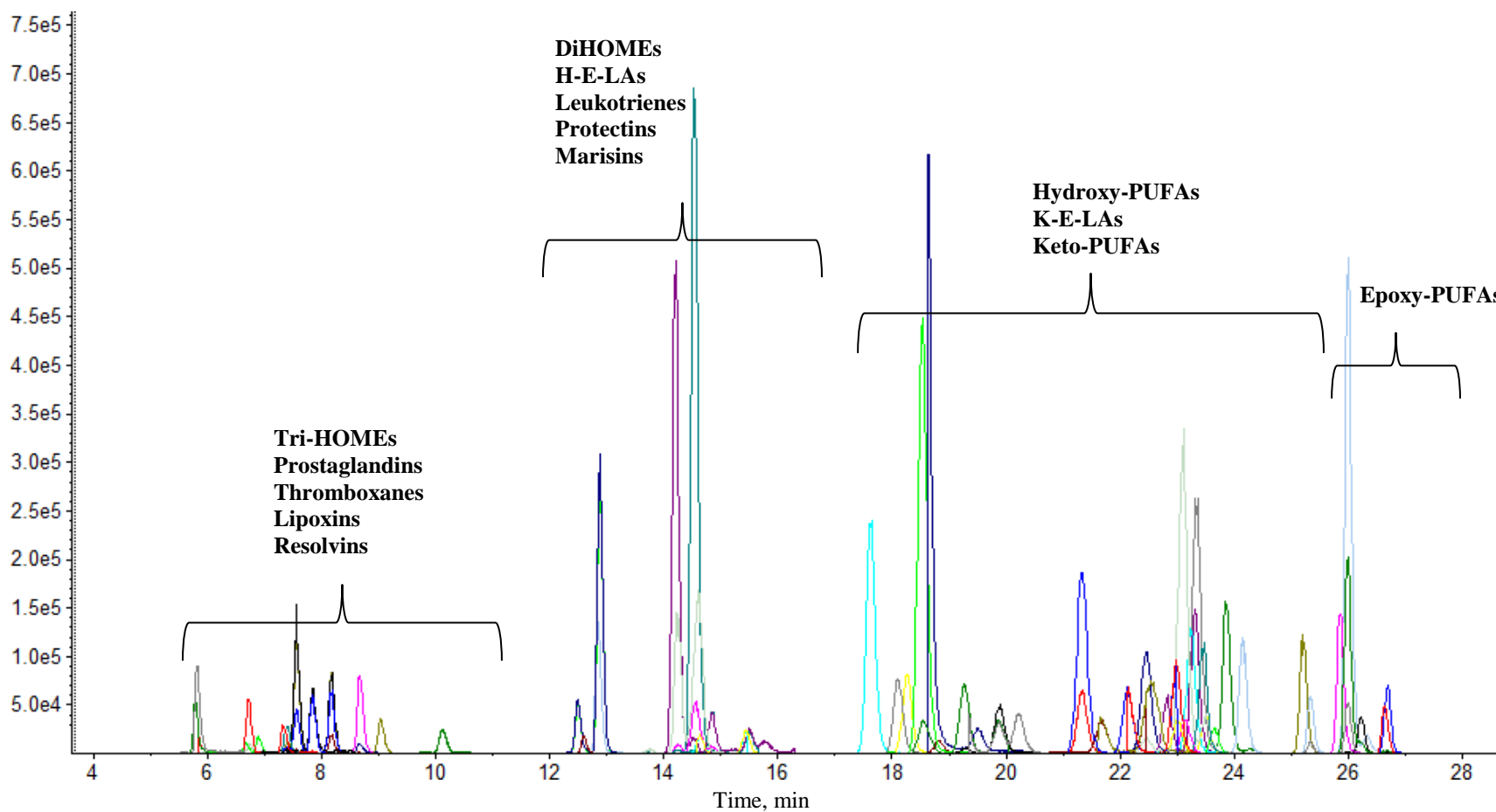
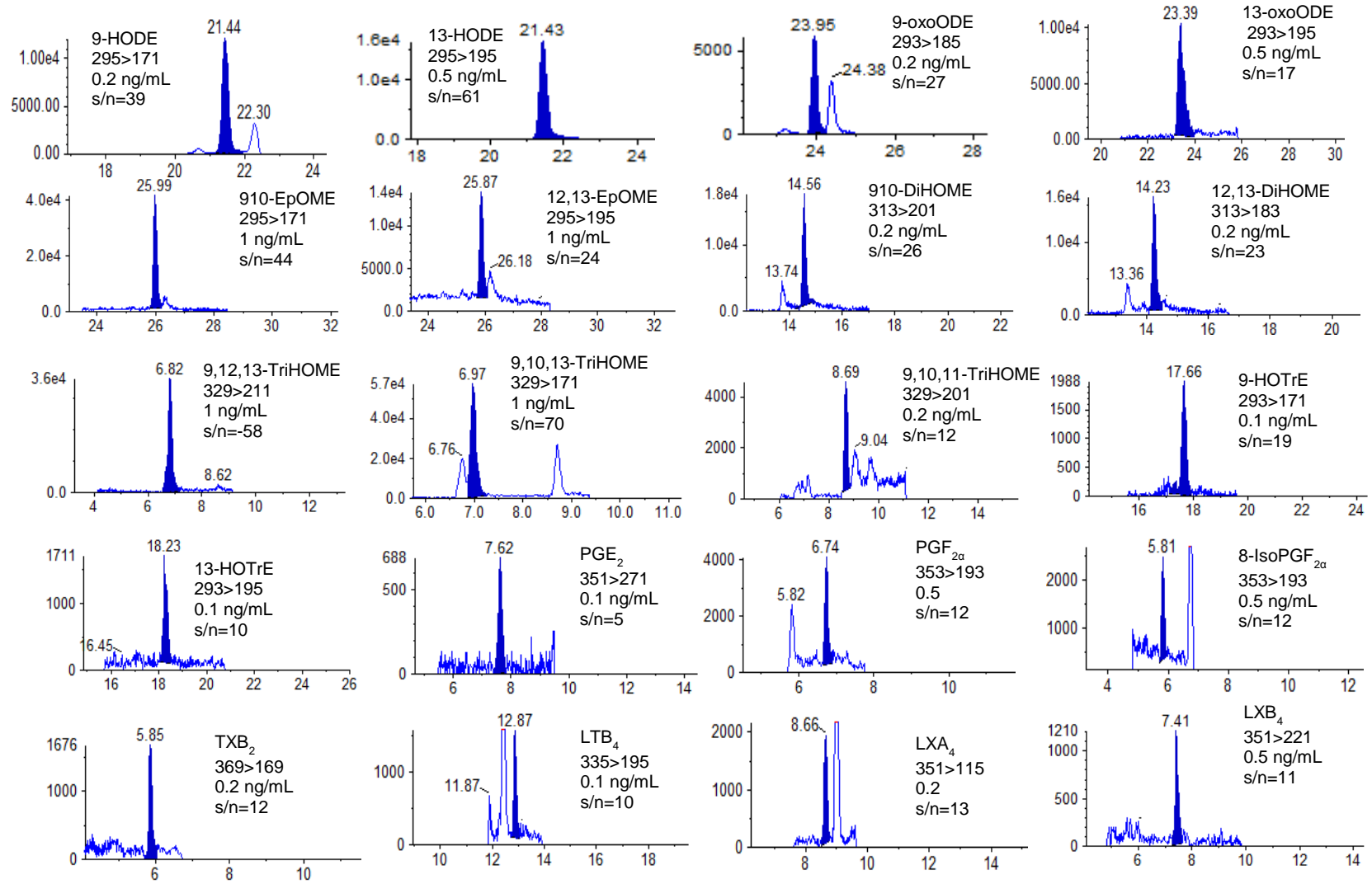
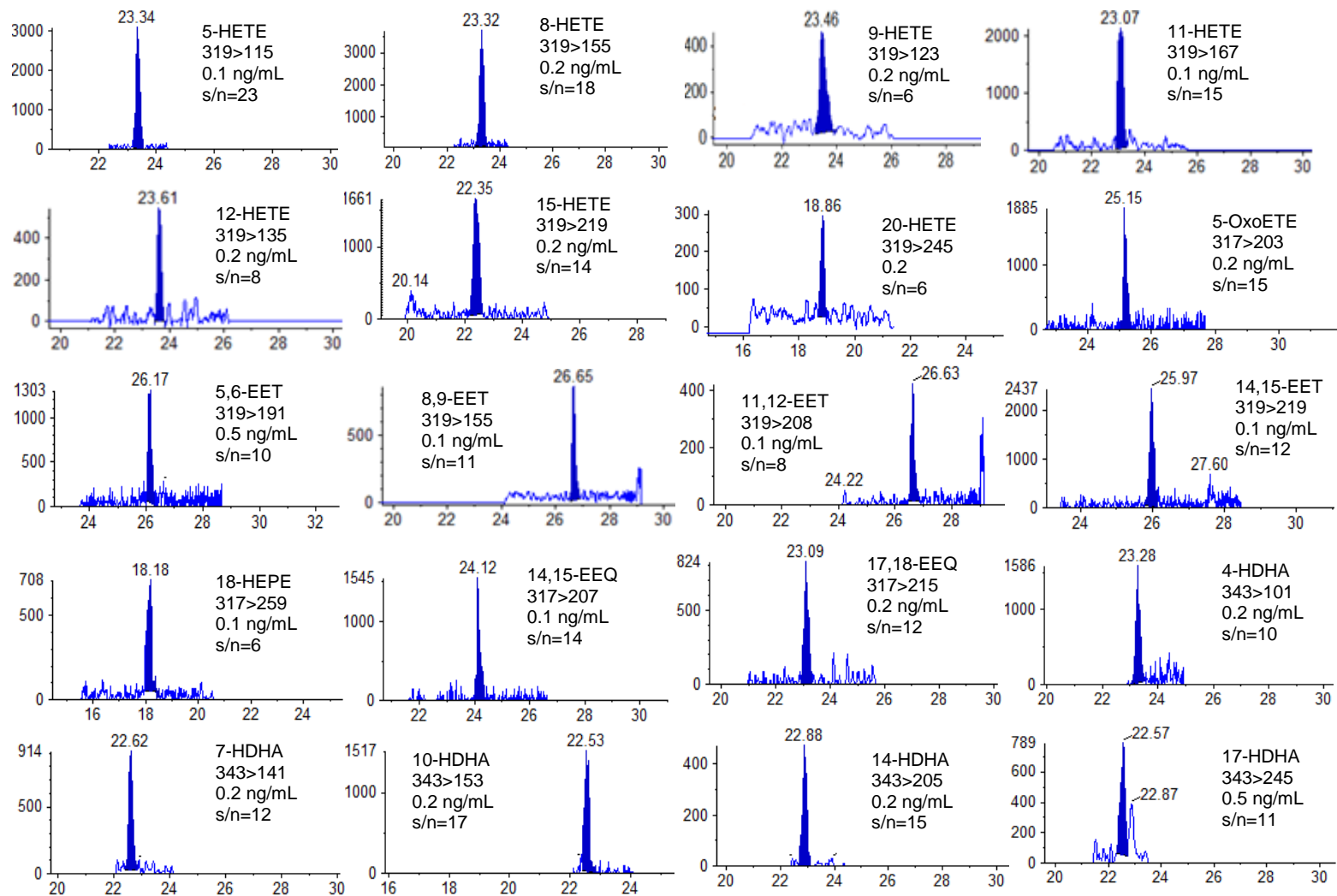


Fig. S1. Representative total ion chromatogram of MRM analysis of 57 targeted oxylipins in the standard mixture. PUFA, polyunsaturated fatty acid; HODE, hydroxy-octadecadienoic acid; DiHOME, dihydroxy-octadecenoic acid, TriHOME, trihydroxy-octadecenoic acid; H-E-LA, hydroxyl-epoxy-octadecenoic acid; K-E-LA, keto-epoxy-octadecenoic acid. A ZorBAX RRHD Eclipse Plus C18 column (100 mm x 4.6 mm; 1.8 μ m) was used for chromatographic separation. The mobile phase A consisted of 12 mM ammonium acetate solution and acetic acid (100:0.02 v/v), and B contained 12 mM ammonium acetate and was composed of acetonitrile/water/acetic acid (90:10:0.02, v/v/v). The flow rate was 0.5 mL/min. Experimental details in Section of Liquid chromatography and mass spectrometry.





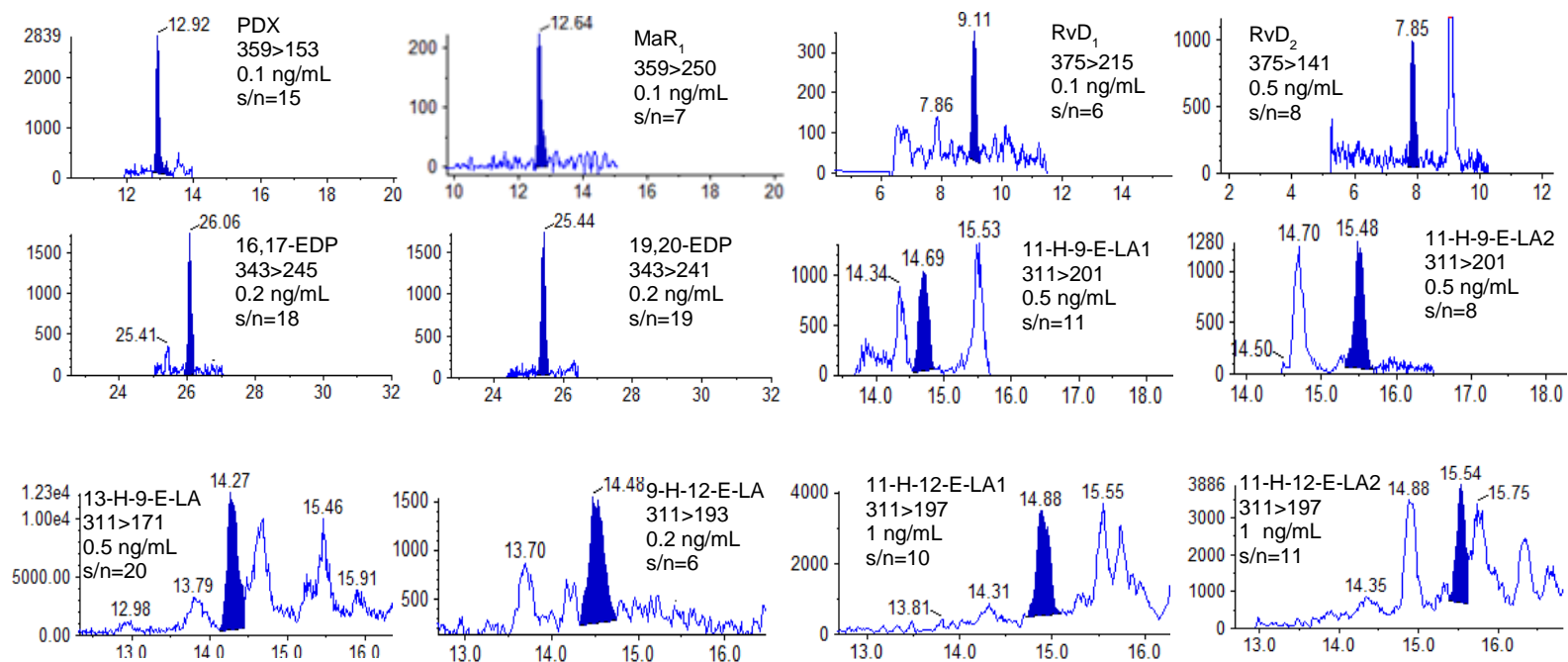


Fig. S2. The representative MRM chromatograms of oxylipins at the LLOQ concentrations. The separation condition, UPLC gradient, sample preparation are described in Method section.