Supplementary Methods

1. Chromatographic fingerprint and multiple ingredients quantification of MLWE

1.1. Chromatographic conditions

The chromatographic separation was carried out on a ZORBAX C18 column (250 × 4.6 mm, 5 μm) maintained at 35 ºC. The mobile phase was composed of 0.1% formic acid methanol solution (A) and 0.02% formic acid water solution (B), and the gradient program was conducted as follows: 0-10 min, 95%-90% B; 10-15 min, 90%-85% B; 15-30 min, 85%-75% B; 30-55 min, 75%-55% B; 55-60 min, 55%-30% B; 60-65 min, 30%-15% B. The system was equilibrated for 6 min in the initial conditions before next injection. Flow rate was 0.8 mL/min and injection volume was 10 μL. The autosampler was set at 4 °C. The detection wavelength was 254 nm.

1.2. Chromatographic fingerprint analysis

The fingerprint analysis was operated through a software Similarity Evaluation System for Chromatographic Fingerprint of Traditional Chinese Medicine (Version 2012A). The chromatographic peaks with total areas more than 90% of the whole area and single areas more than 10% of the whole area in one chromatogram were selected as “common peaks”. The similarity indexes based on those “common peaks” were calculated by mean fusion vector method, and the similarity analysis was performed for 5 batches of MLWE prepared by different operators at different times.

1.3. Multiple ingredients quantification

The validated HPLC method was used to quantify 6 characteristic peaks identified as protocatechuic acid, neochlorogenic acid, chlorogenic acid, cryptochlorogenic acid, rutin and astragalin by the comparison of reference standards. The contents of 6 analytes in 5 batches of MLWE were calculated by their accompanying calibration curves obtained at the same day.

2. Determination of major components

2.1. Total phenolic acids

A 1-mL aliquot of MLWE solutions (1 mg/mL, prepared with 50% ethanol) was mixed with 5 mL of 10% Folin-Phenol. After reacting for 5 min, 4 mL of 7.5% sodium carbonate solution was then added. After placing for 1 h, the absorbance was measured by spectrophotometer at 760 nm. The concentration was calculated with the standard curve plotted with the standard reference of gallic acid.

2.2. Total flavonoids

A 1-mL aliquot of MLWE solutions (1 mg/mL, prepared with 60% ethanol) was mixed with 4.0 mL of 5% sodium nitrite solution. After leaving for 6 min, 0.4 mL of 10% aluminum nitrate solution was then added. After placing for 15 min, 1 mL of 4% sodium hydroxide solution was added. The absorbance was measured by spectrophotometer at 510 nm, and the concentration was calculated with the standard curve plotted with the standard reference of rutin.

2.3. Total polysaccharides

A 1-mL aliquot of MLWE solutions (1 mg/mL, prepared with distilled water) was in sequence added with 1 mL of 5% phenol solution and then 5 mL of concentrated sulfuric acid. After heating in a boiling water bath for 10 min and then cooling to room temperature with ice water, the absorbance was measured by spectrophotometer at 485 nm, and the concentration was calculated with the standard curve plotted with the standard reference of glucose.

3. Identification of chemical ingredients in MLWE by two dimensional liquid phase chromatography coupled with quadrupole/time of flight mass spectrometry

The D1 LC (HILIC) was conducted on a Waters XBridge Amide column (2.1 mm × 150 mm, 3.5 mm). The mobile phase consisted of 0.1% formic acid (A) and acetonitrile (B), and a gradient elution program was used: 0 min, 90% B; 10 min, 60% B. The flow rate was 0.4 mL/min, and the column temperature was 35ºC. The detection wavelength was 254 nm. From 1 to 10 min, a total of 10 fractions were collected with a one-min interval for the next D2 LC analysis.

The D2 LC (RPLC) was separated on an Agilent Eclipse Plus C18 column (4.6 mm × 100 mm, 3.5 mm), and a binary mobile phase composed of 0.1% formic acid (A) and methanol (B) was used following a gradient elution program: 0 min, 5% B; 30 min, 95% B. The flow rate was 1.0 mL/min, and the column temperature was 35ºC. The detection wavelength was 254 nm.

An Agilent 6550 qTOF mass spectrometer equipped with an electrospray interface (ESI) was coupled to the D2 LC system, and the ion source was operated in the negative ion mode. The MS parameters were set as follows: ionization mode, Dual AJS ESI (-); reference ion, 112.98 and 1033.98; capillary voltage, 3500 V; drying temperature, 280ºC; dry gas flow, 12 L/min; atomizer pressure, 28 psig; sheath temperature, 350ºC; sheath gas flow, 12 L/min; scan range, m/z 50–1500; cataclastic voltage, 300 V; collision energy, 15 and 45 eV.

Supplementary Results

Table S1 The formulae of high fat and high sucrose diet and normal control diet

Formula	High fat and high sucrose diet		Normal control diet	
	Mass (%)	**Calorie (%)**	**Mass (%)**	**Calorie (%)**
Protein	26.2	20.0	19.2	20.0
Carbohydrate	0	0	60.8	62.2
Sucrose	25.0	19.1	6.5	6.8
Fat	34.9	59.9	4.3	10.0
Others	13.9	1.0	9.2	1.0
Ingredient	**Mass (g)**	**Calorie (Kcal)**	**Mass (g)**	**Calorie (Kcal)**
Casein, 30 Mesh	200	800	200	800
L-Cystine	3	12	3	12
Corn Starch	0	0	506.2	2024.8
Maltodextrin 10	0	0	125	500
Sucrose	193.8	775.2	68.8	275.2
Cellulose, BW200	50	0	50	0
Soybean Oil	25	225	25	225
Lard	245	2205	20	180
Mineral Mix S10026	10	0	10	0
DiCalcium Phosphate	13	0	13	0
Calcium Carbonate	5.5	0	5.5	0
Potassium Citrate, 1 H_2O	16.5	0	16.5	0
Vitamin Mix V10001	10	40	10	40
Choline Bitartrate	2	0	2	0
FD&C Blue Dye #1	0.05	0	0.01	0
FD&C Red Dye #1	0	0	0	0
FD&C Yellow Dye #1	0	0	0.04	0
Total	773.85	4057.2	1055.05	4057

Table S2 Information of targeted103 lipid mediators including 4 polyunsaturated fatty acids (PUFAs) and 99 oxylipins.

No	Lipids (abbreviation)	Lipids (full name)	Formula	CAS No.	Precursor (m/z)	Fragment (m/z)	Polarity
1	±11(12)-EET	±11,(12)-epoxy-5Z,8Z,14Z-eicosatrienoic acid	$C_{20}H_{32}O_3$	123931-40-8	319.0	167.6	Negative
2	±11,12-DiHETrE	±11,12-dihydroxy-5Z,8Z,14Z-eicosatrienoic acid	$C_{20}H_{34}O_4$	/	337.0	167.4	Negative
3	±11-HDoHE	±11-hydroxy-4Z,7Z,9E,13Z,16Z,19Z-docosahexaenoic acid	$C_{22}H_{32}O_3$	87018-59-5	343.0	165.6	Negative
4	±11-HEPE	±11-hydroxy-5Z,8Z,12E,14Z,17Z-eicosapentaenoic acid	$C_{20}H_{30}O_3$	99217-78-4	317.0	167.7	Negative
5	±12(13)-DiHOME	±12,13-dihydroxy-9Z-octadecenoic acid	$C_{18}H_{34}O_4$	263399-35-5	313.1	295.1	Negative
6	±12(13)-EpOME	±12(13)epoxy-9Z-octadecenoic acid	$C_{18}H_{32}O_3$	/	295.0	195.5	Negative
7	±13-HDoHE	±13-hydroxy-4Z,7Z,10Z,14E,16Z,19Z-docosahexaenoic acid	$C_{22}H_{32}O_3$	90780-53-3	343.0	193.5	Negative
8	±14(15)-EET	±14(15)-epoxy-5Z,8Z,11Z-eicosatrienoic acid	$C_{20}H_{32}O_3$	81276-03-1	319.0	219.1	Negative
9	±14(15)-EpETE	±14(15)-epoxy-5Z,8Z,11Z,17Z-eicosatetraenoic acid	$C_{20}H_{30}O_3$	131339-24-7	317.0	207.4	Negative
10	±14,15-DiHETrE	±14,15-dihydroxy-5Z,8Z,11Z-eicosatrienoic acid	$C_{20}H_{34}O_4$	/	337.0	207.2	Negative
11	±16,17-EpDPE	±16,17-epoxy-4Z,7Z,10Z,13Z,19Z-docosapentaenoic acid	$C_{22}H_{32}O_3$	155073-46-4	343.0	233.3	Negative
12	±17(18)-EpETE	±17,18-epoxy-5Z,8Z,11Z,14Z-eicosatetraenoic acid	$C_{20}H_{30}O_3$	/	317.0	255.0	Negative
13	±18-HETE	±18-hydroxy-5Z,8Z,11Z,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_3$	133268-58-3	319.0	261.2	Negative
14	±19(20)-DiHDPA	±19,20-dihydroxy-4Z,7Z,10Z,13Z,16Z-docosapentaenoic acid	$C_{22}H_{34}O_4$	/	360.9	273.1	Negative
15	±19,20-EpDPE	±19,20-epoxy-4Z,7Z,10Z,13Z,16Z-docosapentaenoic acid	$C_{22}H_{32}O_3$	/	343.0	281.3	Negative
16	±20-HDoHE	±20-hydroxy-4Z,7Z,10Z,13Z,16Z,18E-docosahexaenoic acid	$C_{22}H_{32}O_3$	90906-41-5	343.0	281.2	Negative
17	±5,6-DiHETrE	±5,6-dihydroxy-8Z,11Z,14Z-eicosatrienoic acid	$C_{20}H_{34}O_4$	213382-49-1	337.0	319.2	Negative
18	±5-iso PGF2α-VI	(8β)-5,9α,11α-trihydroxy-prosta-6E,14Z-dien-1-oic acid	$C_{20}H_{34}O_5$	179094-11-2	353.0	335.0	Negative
19	±8(9)-EET	±8,9-epoxy-5Z,11Z,14Z-eicosatrienoic acid	$C_{20}H_{32}O_3$	/	319.0	301.2	Negative
20	±8,9-DiHETrE	±8,9-dihydroxy-5Z,11Z,14Z-eicosatrienoic acid	$C_{20}H_{34}O_4$	192461-96-4	337.0	185.5	Negative
21	±8-HDoHE	±8-hydroxy-4Z,6E,10Z,13Z,16Z,19Z-docosahexaenoic acid	$C_{22}H_{32}O_3$	90780-54-4	343.0	189.5	Negative
22	±9(10)-DiHOME	±9,10-dihydroxy-12Z-octadecenoic acid	$C_{18}H_{34}O_4$	263399-34-4	313.1	277.4	Negative
23	±9(10)-EpOME	±9,10-epoxy-12Z-octadecenoic acid	$C_{18}H_{32}O_3$	65167-83-1	295.0	277.2	Negative
24	10-Nitrooleic Acid	10-nitro-9E-octadecenoic acid	$C_{18}H_{33}NO_4$	875685-46-4	326.0	279.2	Negative
25	11-dehydro TXB2	9α,15S-dihydroxy-11-oxothromba-5Z,13E-dien-1-oic acid	$C_{20}H_{32}O_6$	67910-12-7	366.8	305.1	Negative
26	11S-HETE	11S-hydroxy-5Z,8Z,12E,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_3$	54886-50-9	319.0	167.6	Negative
27	11β-13,14-dihydro-15-keto PGF2α	9α,11β-dihydroxy-15-oxo-prost-5Z-en-1-oic acid	$C_{20}H_{34}O_5$	107615-77-0	353.0	195.5	Negative
28	11β-PGE2	9-oxo-11β,15S-dihydroxy-prosta-5Z,13E-dien-1-oic acid	$C_{20}H_{32}O_5$	38310-90-6	350.9	271.1	Negative
29	11β-PGF2α	9α,11β,15S-trihydroxy-prosta-5Z,13E-dien-1-oic acid	$C_{20}H_{34}O_5$	38432-87-0	353.0	309.1	Negative
30	12-oxo LTB4	5S-hydroxy-12-oxo-6Z,8E,10E,14Z-eicosatetraenoic acid	$C_{20}H_{30}O_4$	136696-10-1	333.0	179.5	Negative
31	12-OxoETE	12-oxo-5Z,8Z,10E,14Z-eicosatetraenoic acid	$C_{20}H_{30}O_3$	108437-64-5	317.1	273.0	Negative
32	12S-HEPE	12S-hydroxy-5Z,8Z,10E,14Z,17Z-eicosapentaenoic acid	$C_{20}H_{30}O_3$	116180-17-7	317.0	179.6	Negative
33	12S-HETE	12S-hydroxy-5Z,8Z,10E,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_3$	54397-83-0	319.0	179.4	Negative
34	12S-HHTrE	12S-hydroxy-5Z,8E,10E-heptadecatrienoic acid	$C_{17}H_{28}O_3$	54397-84-1	279.2	179.4	Negative
35	13,14-dihydro PGF2α	9α,11α,15S-trihydroxy-prost-5Z-en-1-oic acid	$C_{20}H_{36}O_5$	27376-74-5	354.8	311.0	Negative

Table S2: Continued

No	Lipids (abbreviation)	Lipids (full name)	Formula	CAS No.	Precursor (m/z)	Fragment (m/z)	Polarity
36	13,14-dihydro-15-keto PGD2	9α-hydroxy-11,15-dioxo-prost-5Z-en-1-oic acid	$C_{20}H_{32}O_5$	59894-07-4	350.9	333.0	Negative
37	13,14-dihydro-15-keto PGF2α	9α,11α-dihydroxy-15-oxo-prost-5Z-en-1-oic acid	$C_{20}H_{34}O_5$	27376-76-7	353.0	183.5	Negative
38	13-OxoODE	13-oxo-9Z,11E-octadecadienoic acid	$C_{18}H_{30}O_3$	54739-30-9	293.2	195.3	Negative
39	13S-HODE	13S-hydroxy-9Z,11E-octadecadienoic acid	$C_{18}H_{32}O_3$	29623-28-7	295.2	195.5	Negative
40	13S-HOTrE	13S-hydroxy-9Z,11E,15Z-octadecatrienoic acid	$C_{18}H_{30}O_3$	87984-82-5	293.1	195.5	Negative
41	13S-HOTrE(γ)	13S-hydroxy-6Z,9Z,11E-octadecatrienoic acid	$C_{18}H_{30}O_3$	74784-20-6	293.1	193.4	Negative
42	14,15-LTC4	15S-hydroxy-14R-(S-glutathionyl)-5Z,8Z,10E,12E-eicosatetraenoic acid	$C_{30}H_{47}N_3O_9S$	75290-60-7	623.7	272.2	Negative
43	14,15-LTD4	S-[(1R,2E,4E,6Z,9Z)-13-carboxy-1-[(1S)-1-hydroxyhexyl]-2,4,6,9-tridecatetraen-1-yl]-L-cysteinyl-glycine	$C_{25}H_{40}N_2O_6S$	75290-64-1	495.0	177.6	Negative
44	14,15-LTE4	15S-hydroxy-14R-(S-cysteinyl)-5Z,8Z,10E,12E-eicosatetraenoic acid	$C_{23}H_{37}NO_5S$	1000852-57-2	438.0	351.0	Negative
45	15-deoxy-Δ12,14-PGD2	9α-hydroxy-11-oxo-prosta-5Z,12E,14E-trien-1-oic acid	$C_{20}H_{30}O_4$	85235-11-6	333.0	315.2	Negative
46	15-deoxy-Δ12,14-PGJ2	11-oxo-prosta-5Z,9,12E,14E-tetraen-1-oic acid	$C_{20}H_{28}O_3$	87893-55-8	315.1	270.9	Negative
47	15-keto PGE2	9,15-dioxo-11α-hydroxy-prosta-5Z,13E-dien-1-oic acid	$C_{20}H_{30}O_5$	26441-05-4	348.8	331.0	Negative
48	15-keto PGF1α	9α,11α-dihydroxy-15-oxo-prost-13E-en-1-oic acid	$C_{20}H_{34}O_5$	21562-58-3	353.0	193.4	Negative
49	15-OxoEDE	15-oxo-11Z,13E-eicosadienoic acid	$C_{20}H_{34}O_3$	105835-44-7	321.0	223.5	Negative
50	15-OxoETE	15-oxo-5Z,8Z,11Z,13E-eicosatetraenoic acid	$C_{20}H_{30}O_3$	81416-72-0	317.1	273.0	Negative
51	15S-HEPE	15S-hydroxy-5Z,8Z,11Z,13E,17Z-eicosapentaenoic acid	$C_{20}H_{30}O_3$	86282-92-0	317.0	219.4	Negative
52	15S-HETrE	15S-hydroxy-8Z,11Z,13E-eicosatrienoic acid	$C_{20}H_{34}O_3$	92693-02-2	321.1	303.2	Negative
53	16S-HETE	16S-hydroxy-5Z,8Z,11Z,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_3$	183509-23-1	319.0	301.2	Negative
54	17S-HETE	17S-hydroxy-5Z,8Z,11Z,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_3$	183509-25-3	319.0	301.2	Negative
55	19R-hydroxy PGE2	9-oxo-11α,15S,19R-trihydroxy-prosta-5Z,13E-dien-1-oic acid	$C_{20}H_{32}O_6$	64625-54-3	366.9	330.9	Negative
56	19R-hydroxy PGF2α	9α,11α,15S,19R-tetrahydroxy-prosta-5Z,13E-dien-1-oic acid	$C_{20}H_{34}O_6$	64625-53-2	368.8	325.0	Negative
57	19S-HETE	19S-hydroxy-5Z,8Z,11Z,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_3$	115461-40-0	319.0	275.2	Negativ

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58	1a,1b-dihomo PGE2	9-oxo-11α,15S-dihydroxy-1a,1b-dihomo-prosta-5Z,13E-dien-1-oic acid	$C_{22}H_{36}O_5$	26198-80-1	378.9	343.1	Negative
59	1a,1b-dihomo PGF2α	9α,11α,15S-trihydroxy-1a,1b-dihomo-prosta-5Z,13E-dien-1-oic acid	$C_{22}H_{38}O_5$	57944-39-5	380.8	337.0	Negative
60	2,3-dinor TXB2	9α,11,15S-trihydroxy-2,3-dinor-thromba-5Z,13E-dien-1-oic acid	$C_{18}H_{30}O_6$	63250-09-9	340.8	167.3	Negative
61	2,3-dinor-11β-PGF2α	9α,11β,15S-trihydroxy-2,3-dinor-prosta-5Z,13E-dien-1-oic acid	$C_{18}H_{30}O_5$	240405-20-3	325.0	237.2	Negative
62	2,3-dinor-8-iso-PGF2α	9α,11α,15S-trihydroxy-2,3-dinor-(8β)-prosta-5Z,13E-dien-1-oic acid	$C_{18}H_{30}O_5$	221664-05-7	325.0	237.2	Negative
63	20-carboxy LTB4	5S,12R-dihydroxy-6Z,8E,10E,14Z-eicosatetraene-1,20-dioic acid	$C_{20}H_{30}O_6$	80434-82-8	364.9	346.6	Negative
64	20-HETE	20-hydroxy-5Z,8Z,11Z,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_3$	79551-86-3	319.0	301.2	Negative
65	20-hydroxy LTB4	5S,12R,20-trihydroxy-6Z,8E,10E,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_5$	79516-82-8	350.9	195.5	Negative
66	5-OxoETE	5-oxo-6E,8Z,11Z,14Z-eicosatetraenoic acid	$C_{20}H_{30}O_3$	106154-18-1	317.1	203.6	Negative
67	5S,6R-DiHETE	5S,6R-dihydroxy-7E,9E,11Z,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_4$	82948-88-7	335.0	317.2	Negative
68	5S-HEPE	5S-hydroxy-6E,8Z,11Z,14Z,17Z-eicosapentaenoic acid	$C_{20}H_{30}O_3$	92008-51-0	317.0	255.0	Negative
69	5S-HETrE	5S-hydroxy-6E,8Z,11Z-eicosatrienoic acid	$C_{20}H_{34}O_3$	195061-94-0	321.1	303.2	Negative
70	6-keto PGF1α	6-oxo-9α,11α,15S-trihydroxy-prost-13E-en-1-oic acid	$C_{20}H_{34}O_6$	58962-34-8	368.8	245.2	Negative

Table S2: Continued

No.	Lipids (abbreviation)	Lipids (full name)	Formula	CAS No.	Precursor (m/z)	Fragment (m/z)	Polarity
71	6S-LXA4	5S,6S,15S-trihydroxy-7E,9E,11Z,13E-eicosatetraenoic acid	$C_{20}H_{32}O_5$	94292-80-5	350.9	235.4	Negative
72	6-trans LTB4	5S,12R-dihydroxy-6E,8E,10E,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_4$	71652-82-9	335.0	195.5	Negative
73	8-iso PGF2α	9α,11α,15S-trihydroxy-(8β)-prosta-5Z,13E-dien-1-oic acid	$C_{20}H_{34}O_5$	27415-26-5	353.0	193.5	Negative
74	8-iso-15-keto PGF2β	9β,11α-dihydroxy-15-oxo-(8β)-prosta-5Z,13E-dien-1-oic acid	$C_{20}H_{32}O_5$	1621482-36-7	350.7	315.0	Negative
75	8S,15S-DiHETE	8S,15S-dihydroxy-5Z,9E,11Z,13E-eicosatetraenoic acid	$C_{20}H_{32}O_4$	80234-65-7	335.0	235.5	Negative
76	8S-HETrE	8S-hydroxy-9E,11Z,14Z-eicosatrienoic acid	$C_{20}H_{34}O_3$	889573-69-7	321.1	303.2	Negative
77	9-Nitrooleic Acid	9-nitro-9E-octadecenoic acid	$C_{18}H_{33}NO_4$	875685-44-2	326.0	308.0	Negative
78	9-OxoODE	9-oxo-10E,12Z-octadecadienoic acid	$C_{18}H_{30}O_3$	54232-59-6	293.2	185.5	Negative
79	9R-HETE	9R-hydroxy-5Z,7E,11Z,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_3$	107656-14-4	319.0	167.6	Negative
80	9S-HODE	9S-hydroxy-10E,12Z-octadecadienoic acid	$C_{18}H_{32}O_3$	73543-67-6	295.2	277.3	Negative
81	9S-HOTrE	9S-hydroxy-10E,12Z,15Z-octadecatrienoic acid	$C_{18}H_{30}O_3$	89886-42-0	293.1	275.2	Negative
82	ARA	5Z,8Z,11Z,14Z-eicosatetraenoic acid	$C_{20}H_{32}O_2$	506-32-1	303.2	259.2	Negative
83	DHA	4Z,7Z,10Z,13Z,16Z,19Z-docosahexaenoic acid	$C_{22}H_{32}O_2$	6217-54-5	327.0	283.3	Negative
84	DTA	7Z,10Z,13Z,16Z-docosatetraenoic acid	$C_{22}H_{36}O_2$	28874-58-0	331.1	287.3	Negative
85	EPA	5Z,8Z,11Z,14Z,17Z-eicosapentaenoic acid	$C_{20}H_{30}O_2$	10417-94-4	301.0	257.2	Negative
86	LTE4	5S-hydroxy-6R-(S-cysteinyl)-7E,9E,11Z,14Z-eicosatetraenoic acid	$C_{23}H_{37}NO_5S$	75715-89-8	438.0	333.0	Negative
87	LXA5	5S,6R,15S-trihydroxy-7E,9E,11Z,13E,17Z-eicosapentaenoic acid	$C_{20}H_{30}O_5$	110657-98-2	348.7	215.4	Negative
88	PGA2	9-oxo-15S-hydroxy-prosta-5Z,10,13E-trien-1-oic acid	$C_{20}H_{30}O_4$	13345-50-1	333.0	315.2	Negative
89	PGB2	9-oxo-15S-hydroxy-prosta-5Z,8(12),13E-trien-1-oic acid	$C_{20}H_{30}O_4$	13367-85-6	333.0	175.5	Negative
90	PGD1	9α,15S-dihydroxy-11-oxo-prost-13E-en-1-oic acid	$C_{20}H_{34}O_5$	17968-82-0	353.0	235.3	Negative
91	PGD2	9α,15S-dihydroxy-11-oxo-prosta-5Z,13E-dien-1-oic acid	$C_{20}H_{32}O_5$	41598-07-6	350.7	271.2	Negative
92	PGD3	9α,15S-dihydroxy-11-oxo-prosta-5Z,13E,17Z-trien-1-oic acid	$C_{20}H_{30}O_5$	71902-47-1	348.8	269.3	Negative
93	PGE1	9-oxo-11α,15S-dihydroxy-prost-13E-en-1-oic acid	$C_{20}H_{34}O_5$	745-65-3	353.0	317.0	Negative
94	PGE3	9-oxo-11α,15S-dihydroxy-prosta-5Z,13E,17Z-trien-1-oic acid	$C_{20}H_{30}O_5$	802-31-3	349.0	269.2	Negative
95	PGF1α	9α,11α,15S-trihydroxy-prost-13E-en-1-oic acid	$C_{20}H_{36}O_5$	745-62-0	354.8	311.0	Negative
96	PGF2α	9α,11α,15S-trihydroxy-prosta-5Z,13E-dien-1-oic acid	$C_{20}H_{34}O_5$	551-11-1	353.0	309.1	Negative
97	PGF3α	9α,11α,15S-trihydroxy-prosta-5Z,13E,17Z-trien-1-oic acid	$C_{20}H_{32}O_5$	745-64-2	350.9	307.2	Negative
98	PGJ2	11-oxo-15S-hydroxy-prosta-5Z,9,13E-trien-1-oic acid	$C_{20}H_{30}O_4$	60203-57-8	333.0	315.2	Negative
99	tetranor-12S-HETE	8S-hydroxy-4Z,6E,10Z-hexadecatrienoic acid	$C_{16}H_{26}O_3$	121842-79-3	265.2	165.6	Negative
100	TXB1	9,11,15-trihydroxy-thrombox-13-en-1-oic acid	$C_{20}H_{36}O_6$	64626-32-0	370.9	171.5	Negative
101	TXB2	9α,11,15S-trihydroxythromba-5Z,13E-dien-1-oic acid	$C_{20}H_{34}O_6$	54397-85-2	368.9	169.6	Negative
102	TXB3	9α,11,15S-trihydroxy-thromba-5Z,13E,17Z-trien-1-oic acid	$C_{20}H_{32}O_6$	71953-80-5	366.8	169.6	Negative
103	Δ17-6-keto PGF1α	6-oxo-9α,11α,15S-trihydroxy-prosta-13E,17Z-dien-1-oic acid	$C_{20}H_{32}O_6$	68324-95-8	366.7	163.0	Negative

Table S3 The similarities of 5 batches of MLWE prepared by different operators at different times

MLWE	S1	S2	S3	S4	S5	Reference fingerprint
S1	1.000	0.999	0.999	0.999	0.999	1.000
S2	0.999	1.000	1.000	1.000	1.000	1.000
S3	0.999	1.000	1.000	1.000	1.000	1.000
S4	0.999	1.000	1.000	1.000	0.999	1.000
S5	0.999	1.000	1.000	0.999	1.000	1.000
Reference fingerprint	1.000	1.000	1.000	1.000	1.000	1.000

S1~S5 represent 5 batches of MLWE prepared by different operators at different times, respectively.

Table S4 The contents of major components and 6 analytes in MLWE and oral dose of mice (n=5)

Analytes	Calibration curves	R^2	Linear range (μg/mL)	Contents (mg/g)	RSD%	Daily intake (mg/kg body weight)
Total phenolic acids	$y = 0.0109\,x + 0.007$	0.9992	10 - 50	19.32±0.62	3.2	12.87
Total flavonoids	$y = 1.659\,x + 0.0084$	0.9995	50 - 400	24.59±0.76	3.1	16.38
Total polysaccharides	$y = 9.8109\,x + 0.0724$	0.9988	20 -140	73.12±1.67	2.3	48.68
Protocatechuic acid	$y = 20563x - 323956$	0.9981	15 -300	0.48±0.01	2.1	0.32
Neochlorogenic acid	$y = 1974.2x - 37168$	0.9982	25 - 810	6.20±0.21	3.4	4.13
Chlorogenic acid	$y = 2111x - 97845$	0.9985	50 -1210	6.44±0.19	3.0	4.29
Cryptochlorogenic acid	$y = 2861.6x - 51202$	0.9989	25 -810	6.08±0.18	3.0	4.05
Rutin	$y = 12093x - 308545$	0.9962	12 - 400	2.05±0.05	2.4	1.37
Astragalin	$y = 11671x - 246830$	0.9967	13 - 420	1.01±0.02	2.0	0.67

S1~S5 represent 5 batches of MLWE prepared by different operators at different times, respectively.

Table S5 Characterization of selected chemical constituents in MLWE by two-dimensional liquid phase chromatography coupled with Q/TOF MS/MS

No.	Fraction	t_{R2} (min)	Formula	[M-H]$^-$ (m/z)			Identification	Major fragment ions (m/z)
				Predicted	Measured	Error (ppm)		
1*	1	1.371	$C_{15}H_{14}O_6$	289.0712	289.0729	5.9	Catechuic acid	205.0330, 179.0578
2*	1	5.282	$C_7H_6O_4$	153.0188	153.0177	-7.2	Protocatechuic acid	109.0291, 136.9490
3*	1	7.844	$C_{10}H_8O_4$	191.0344	191.0335	-4.7	Scopolin	164.0319, 147.9559
4	1	10.948	$C_9H_6O_3$	161.0239	161.0247	5.0	Hydroxycoumarin	117.0289
5	1	11.189	$C_9H_8O_3$	163.0395	163.0399	2.5	*p*-Coumaric acid	146.0302
6*	1	12.085	$C_{25}H_{24}O_{12}$	515.1190	515.1175	-2.9	Isochlorogenic acid A	353.1254, 179.1406
7	1	14.210	$C_{16}H_{18}O_9$	353.0873	353.0881	2.3	1-Caffeoylquinic acid	191.0684, 179.0463, 161.0344, 135.0536
8*	1	14.304	$C_{15}H_{10}O_7$	301.0348	301.0322	-8.6	Quercetin	178.9282, 151.0496
9	1	14.526	$C_{23}H_{22}O_{13}$	505.0982	505.1026	8.7	Quercetin-3-O-(6"-*O*-acetyl)-β-D-glucoside	301.0459, 179.0001, 151.0057
10*	1	14.640	$C_{25}H_{24}O_{12}$	515.1190	515.1207	3.3	Isochlorogenic acid C	353.0944, 191.0433
11	1	15.498	$C_{21}H_{22}O_{11}$	449.1084	449.1094	2.2	Dihydrokaempferol 7-glucoside	287.1727
12	1	16.062	$C_{23}H_{22}O_{12}$	489.1033	489.1076	8.8	Kaempferol-3-O-(6″-*O*-acetyl)-β-D-glucoside	285.0496
13*	2	7.998	$C_{16}H_{18}O_9$	353.0873	353.0846	-7.6	Chlorogenic acid	191.0614, 179.0460, 135.0351
14*	2	8.231	$C_{16}H_{18}O_9$	353.0873	353.0903	8.5	Neochlorogenic acid	353, 161
15*	2	8.246	$C_{16}H_{18}O_9$	353.0873	353.0892	5.4	Cryptochlorogenic acid	191.0617, 179.0457, 135.0376
16*	2	15.435	$C_{21}H_{20}O_{11}$	447.0927	447.0906	-4.7	Astragalin	285.0438, 151.0036
17*	3	7.865	$C_{25}H_{26}O_6$	421.1651	421.1685	8.1	Mulberrin	353.1019, 201.0386, 135.0467
18*	3	14.088	$C_{21}H_{20}O_{12}$	463.0877	463.0917	8.6	Isoquercitrin(quercetin-3-*O*-glucoside)	300.0363, 271.0241, 151.0102
19	3	18.040	$C_{30}H_{26}O_{13}$	593.1295	593.132	4.2	Kaempferol-3-*O*-(6”-p-coumaroyl)-glucoside	285.0337
20*	4	9.081	$C_9H_8O_4$	179.0344	179.0331	-7.3	Caffeic acid	161.1098, 135.0446
21	4	13.582	$C_{27}H_{30}O_{15}$	593.1506	593.1561	9.3	Kaempferol-3-*O*-rutinoside	284.9330, 102.9579
22	5	10.252	$C_{27}H_{30}O_{16}$	609.1456	609.1509	8.7	Quercetin 3-(2’’-glucosyl)-rhamnoside	300.1025, 285.0463
23	5	15.525	$C_{27}H_{30}O_{15}$	593.1506	593.1561	9.3	Kaempferol-7-O-neohesperidoside	285.0505
24	6	8.445	$C_{24}H_{22}O_{15}$	549.0880	549.0911	5.6	Quercetin-3-O-(6"-malonyl)-glucoside	505.0373, 300.9095, 179.0584
25	6	9.063	$C_{27}H_{30}O_{17}$	625.1405	625.1401	-0.6	Quercetin-3,7-diglucoside	301.0398, 151.0051
26*	6	11.927	$C_{27}H_{30}O_{16}$	609.1456	609.1509	8.7	Rutin	301.0498, 285.1097
27	6	13.202	$C_{36}H_{36}O_{17}$	739.1953	739.1884	-9.3	Kaempferol-3-*O*-rutinoside-7-sorboside	575.1684, 284.0420
28	6	14.049	$C_{27}H_{30}O_{16}$	609.1456	609.1515	9.7	Quercetin-3-*O*-glucoside-7-O-rhamnoside	300.9047
29	7	9.070	$C_{27}H_{30}O_{17}$	625.1405	625.1404	-0.2	Quercetin-3-*O*-gentiobioside	301.0460, 151.0050
30	7	10.755	$C_{33}H_{40}O_{20}$	755.2035	755.2103	9.0	Quercetin 3-*O*-(2’’,6’’-di-O-rhamnosyl)-galactoside	300.2035
31	7	12.310	$C_{36}H_{36}O_{18}$	755.1823	755.1868	6.0	Quercetin-3-*O*-*p*- coumaroyl-diglucoside	300.0382
32	8	1.779	$C_{18}H_{14}O_7$	341.0661	341.0657	-1.2	Caffeic anhydride	281.022, 258.9012, 178.9963, 118.9943
33	8	9.329	$C_{33}H_{40}O_{21}$	771.1984	771.2005	2.7	Quercetin-3-*O*-rutinoside-7-*O*-glucoside	609.1608, 301.0403
34	8	10.819	$C_{36}H_{36}O_{18}$	755.1823	755.1845	2.9	Quercetin-3-*O*-2”-(6”-*p*- coumaroylglucosyl)-rhamnoside	300.0958

*Identification by the reference standards.

Table S6 The linearity and ranges, correlation coefficient and limit of detection (LOD) of quantitative 103 lipid mediators.

No.	Compounds	Linearity	R^2	Limit of detection (ng/ mL)	Ranges (ng/ mL)
1	±11(12)-EET	$y = 0.00364\ x^2 + 0.42036\ x + 3.84052\times10^{-4}$	0.9998	0.02	0.04~5.00
2	±11,12-DiHETrE	$y = 0.15093\ x - 6.45618\times10^{-4}$	0.9996	0.04	0.08~5.00
3	±11-HDoHE	$y = 3.88577\times10^{-4}\ x^2 + 0.01272\ x + 2.8643\times10^{-4}$	0.9995	0.08	0.16~20.00
4	±11-HEPE	$y = 6.47517\times10^{-4}\ x^2 + 0.04068\ x + 0.00130$	0.9982	0.08	0.16~20.00
5	±12(13)-DiHOME	$y = 0.06179\ x + 0.00241$	0.9998	0.16	0.31~5.00
6	±12(13)-EpOME	$y = 6.34305\times10^{-4}\ x^2 + 0.02101\ x + 4.44096\times10^{-4}$	0.9993	0.04	0.08~20.00
7	±13-HDoHE	$y = 0.16065\ x + 1.52397\times10^{-4}$	0.9998	0.04	0.08~5.00
8	±14(15)-EET	$y = 5.87707\times10^{-4}\ x^2 + 0.26604\ x + 8.86645\times10^{-5}$	0.9998	0.02	0.04~5.00
9	±14(15)-EpETE	$y = -1.91226\times10^{-4}\ x^2 + 0.18508\ x + 0.00216$	0.9998	0.08	0.16~20.00
10	±14,15-DiHETrE	$y = 0.14943\ x - 4.45914\times10^{-4}$	0.9990	0.04	0.08~5.00
11	±16,17-EpDPE	$y = 0.00119\ x^2 + 0.12017\ x + 8.60370\times10^{-4}$	0.9997	0.02	0.04~20.00
12	±17(18)-EpETE	$y = -0.0011\ x^2 + 0.15277\ x - 2.19255\times10^{-4}$	0.9992	0.16	0.31~20.00
13	±18-HETE	$y = 5.33267\times10^{-4}\ x^2 + 0.04807\ x + 4.56449\times10^{-5}$	0.9990	0.16	0.31~20.00
14	±19(20)-DiHDPA	$y = 0.04368\ x - 0.00109$	0.9997	0.16	0.31~20.00
15	±19,20-EpDPE	$y = 0.35508\ x + 0.00359$	0.9997	0.08	0.16~5.00
16	±20-HDoHE	$y = 3.86602\times10^{-4}\ x^2 + 0.06145\ x + 0.00109$	0.9992	0.08	0.16~20.00
17	±5,6-DiHETrE	$y = 0.04320\ x + 2.99756\times10^{-4}$	0.9997	0.16	0.31~5.00
18	±5-iso PGF2α-VI	$y = -0.00161\ x^2 + 0.12920\ x - 0.00565$	0.9997	0.63	1.25~20.00
19	±8(9)-EET	$y = 6.08571\times10^{-4}\ x^2 + 0.12744\ x + 0.00452$	0.9999	0.16	0.31~20.00
20	±8,9-DiHETrE	$y = 1.25786\times10^{-4}\ x^2 + 0.02639\ x + 5.16208\times10^{-4}$	0.9999	0.04	0.08~20.00
21	±8-HDoHE	$y = 7.01234\times10^{-4}\ x^2 + 0.07984\ x + 9.47556\times10^{-4}$	0.9999	0.08	0.16~5.00
22	±9(10)-DiHOME	$y = -4.90077\times10^{-5}\ x^2 + 0.03333\ x - 9.82612\times10^{-4}$	0.9996	0.16	0.31~20.00
23	±9(10)-EpOME	$y = 0.00531\ x^2 + 0.07528\ x + 0.00357$	0.9999	0.04	0.08~5.00
24	10-Nitrooleic Acid	$y = -0.00237\ x^2 + 0.16948\ x + 4.27261\times10^{-4}$	0.9993	0.08	0.16~5.00
25	11-dehydro TXB2	$y = 0.06085\ x + 0.00237$	0.9997	0.16	0.31~5.00
26	11S-HETE	$y = 0.01888\ x^2 + 0.19647\ x + 0.0014$	0.9993	0.02	0.04~5.00
27	11β-13,14-dihydro-15-keto PGF2α	$y = 0.00119\ x^2 + 0.11065\ x + 0.0334$	0.9999	0.31	0.63~20.00
28	11β-PGE2	$y = -0.02099\ x^2 + 0.39887\ x + 0.00384$	0.9996	0.08	0.16~5.00
29	11β-PGF2α	$y = -0.00148\ x^2 + 0.1172\ x - 0.00624$	0.9999	0.31	0.63~20.00
30	12-oxo LTB4	$y = -2.81168\times10^{-5}\ x^2 + 0.04494\ x - 2.79108\times10^{-4}$	0.9998	0.08	0.16~20.00
31	12-OxoETE	$y = 0.00310\ x^2 + 0.20955\ x + 0.00624$	0.9997	0.08	0.16~5.00
32	12S-HEPE	$y = 5.60644\times10^{-4}\ x^2 + 0.04421\ x + 0.00105$	0.9993	0.31	0.63~20.00
33	12S-HETE	$y = 0.10128\ x - 0.0132$	0.9992	0.02	0.04~5.00
34	12S-HHTrE	$y = 1.21299\times10^{-4}\ x^2 + 0.03940\ x + 2.19510\times10^{-4}$	0.9996	0.04	0.08~20.00
35	13,14-dihydro PGF2α	$y = 0.04525\ x - 0.00965$	0.9991	0.63	1.25~20.00
36	13,14-dihydro-15-keto PGD2	$y = -0.00508\ x^2 + 0.15847\ x + 0.00443$	0.9997	0.08	0.16~5.00
37	13,14-dihydro-15-keto PGF2α	$y = 1.90192\times10^{-4}\ x^2 + 0.121\ x - 0.00113$	0.9996	0.08	0.16~20.00
38	13-OxoODE	$y = 0.04363\ x + 0.00859$	0.9996	0.08	0.16~20.00
39	13S-HODE	$y = 0.12993\ x + 0.00799$	0.9988	0.00	0.01~5.00
40	13S-HOTrE	$y = 3.1197\times10^{-4}\ x^2 + 0.04148\ x + 0.00142$	0.9998	0.04	0.08~20.00
41	13S-HOTrE(γ)	$y = 5.8667\times10^{-5}\ x^2 + 0.01627\ x + 7.68639\times10^{-5}$	0.9996	0.04	0.08~20.00
42	14,15-LTC4	$y = 8.27563\times10^{-6}\ x^2 + 0.00129\ x - 8.68739\times10^{-4}$	0.9989	0.08	0.16~100.00
43	14,15-LTD4	$y = -7.50186\times10^{-6}\ x^2 + 6.88566\times10^{-4}\ x + 1.76236\times10^{-4}$	0.9995	0.04	0.08~20.00
44	14,15-LTE4	$y = -0.00438\ x^2 + 0.08607\ x - 0.01971$	0.9999	0.16	0.31~10.00
45	15-deoxy-Δ12,14-PGD2	$y = 0.00181\ x^2 + 0.1241\ x + 0.00137$	0.9997	0.08	0.16~5.00

Continued Table S6

No.	Compounds	Linearity	Correlation coefficient (R^2)	Limit of detection (ng/ mL)	Ranges (ng/ mL)
46	15-deoxy-Δ12,14-PGJ2	$y = 0.02484\ x^2 + 0.78447\ x + 0.00799$	0.9984	0.02	0.04~5.00
47	15-keto PGE2	$y = 0.2461\ x + 0.0169$	0.9992	0.31	0.63~5.00
48	15-keto PGF1α	$y = -0.01463\ x^2 + 0.30398\ x - 7.8967\times10^{-5}$	0.9997	0.04	0.08~5.00
49	15-OxoEDE	$y = 4.39089\times10^{-4}\ x^2 + 0.02846\ x + 2.14137\times10^{-4}$	0.9997	0.08	0.16~20.00
50	15-OxoETE	$y = 0.00767\ x^2 + 0.23548\ x + 0.02101$	0.9995	0.08	0.16~5.00
51	15S-HEPE	$y = 6.66447\times10^{-4}\ x^2 + 0.03387\ x + 0.00147$	0.9982	0.08	0.16~20.00
52	15S-HETrE	$y = 0.44076\ x - 0.00306$	0.9993	0.02	0.04~5.00
53	16S-HETE	$y = 0.1329\ x - 0.00416$	0.9994	0.16	0.31~5.00
54	17S-HETE	$y = 0.00202\ x^2 + 0.07103\ x + 0.0032$	0.9994	0.16	0.31~5.00
55	19R-hydroxy PGE2	$y = -0.02444\ x^2 + 0.33046\ x - 1.14829\times10^{-4}$	0.9996	0.04	0.08~5.00
56	19R-hydroxy PGF2α	$y = -0.01189\ x^2 + 0.14646\ x + 0.0018$	0.9995	0.08	0.16~5.00
57	19S-HETE	$y = 1.82360\times10^{-4}\ x^2 + 0.02390\ x + 0.00147$	0.9993	0.31	0.63~20.00
58	1a,1b-dihomo PGE2	$y = 0.2172\ x + 0.00143$	0.9995	0.02	0.04~5.00
59	1a,1b-dihomo PGF2α	$y = 0.05805\ x + 0.0012$	0.9992	0.02	0.04~5.00
60	2,3-dinor TXB2	$y = 1.56802\times10^{-4}\ x^2 + 0.02373\ x - 4.4328\times10^{-4}$	0.9983	0.31	0.63~20.00
61	2,3-dinor-11β-PGF2α	$y = -6.6512\times10^{-4}\ x^2 + 0.03862\ x - 9.29904\times10^{-4}$	0.9985	0.31	0.63~20.00
62	2,3-dinor-8-iso-PGF2α	$y = -0.01003\ x^2 + 0.192\ x - 7.26589\times10^{-4}$	0.9994	0.04	0.08~5.00
63	20-carboxy LTB4	$y = -2.05107\times10^{-4}\ x^2 + 0.02526\ x + 4.08164\times10^{-4}$	0.9996	0.08	0.16~20.00
64	20-HETE	$y = 1.76049\times10^{-4}\ x^2 + 0.00934\ x + 4.11238\times10^{-4}$	0.9990	0.63	1.25~20.00
65	20-hydroxy LTB4	$y = -2.24882\times10^{-4}\ x^2 + 0.03107\ x - 1.24671\times10^{-4}$	0.9983	0.16	0.31~20.00
66	5-OxoETE	$y = 0.00189\ x^2 + 0.10128\ x + 0.00389$	0.9997	0.04	0.08~5.00
67	5S,6R-DiHETE	$y = 0.21292\ x + 0.00966$	0.9982	0.08	0.16~5.00
68	5S-HEPE	$y = 0.00356\ x^2 + 0.07992\ x + 1.34005\times10^{-4}$	0.9986	0.08	0.16~5.00
69	5S-HETrE	$y = 0.00249\ x^2 + 0.3434\ x - 0.00373$	0.9997	0.02	0.04~5.00
70	6-keto PGF1α	$y = 0.00835\ x + 0.00154$	0.9996	0.31	0.63~20.00
71	6S-LXA4	$y = 5.98314\times10^{-6}\ x^2 + 0.05154\ x + 0.00174$	0.9998	0.08	0.16~20.00
72	6-trans LTB4	$y = 4.89842\times10^{-4}\ x^2 + 0.12646\ x + 1.29972\times10^{-4}$	0.9998	0.02	0.04~5.00
73	8-iso PGF2α	$y = -1.1124\times10^{-4}\ x^2 + 0.02913\ x - 0.00198$	0.9992	0.16	0.31~20.00
74	8-iso-15-keto PGF2β	$y = -0.00337\ x^2 + 0.04317\ x - 0.00186$	0.9992	0.31	0.63~5.00
75	8S,15S-DiHETE	$y = 8.03507\times10^{-5}\ x^2 + 0.02521\ x + 7.78623\times10^{-4}$	0.9995	0.04	0.08~20.00
76	8S-HETrE	$y = 0.44064\ x - 0.00477$	0.9997	0.02	0.04~5.00
77	9-Nitrooleic Acid	$y = 0.00173\ x^2 + 0.15826\ x + 1.59917\times10^{-4}$	0.9998	0.02	0.04~5.00
78	9-OxoODE	$y = 8.88549\times10^{-5}\ x^2 + 0.12268\ x + 0.01701$	0.9996	0.04	0.08~20.00
79	9R-HETE	$y = 1.47905\times10^{-4}\ x^2 + 0.06329\ x + 9.83906\times10^{-5}$	0.9999	0.31	0.63~20.00
80	9S-HODE	$y = 0.19444\ x + 0.00603$	0.9996	0.00	0.01~5.00
81	9S-HOTrE	$y = 0.00249\ x^2 + 0.15932\ x + 0.00426$	0.9998	0.08	0.16~5.00
82	ARA	$y = 0.10345\ x + 0.03687$	0.9996	0.04	0.08~5.00
83	DHA	$y = 0.29718\ x + 0.12718$	0.9992	0.02	0.04~5.00
84	DTA	$y = 0.04638\ x + 0.00353$	0.9998	0.16	0.31~5.00
85	EPA	$y = 0.15526\ x + 0.00338$	0.9994	0.04	0.08~5.00
86	LTE4	$y = 0.02308\ x + 0.01488$	0.9996	0.16	0.31~20.00
87	LXA5	$y = -9.81728\times10^{-5}\ x^2 + 0.01889\ x + 3.33294\times10^{-4}$	0.9999	0.31	0.63~20.00
88	PGA2	$y = 0.1587\ x + 0.01041$	0.9981	0.31	0.63~5.00

Continued Table S6

No.	Compounds	Linearity	Correlation coefficient (R^2)	Limit of detection (ng/ mL)	Ranges (ng/ mL)
89	PGB2	$y = -2.48603\times10^{-4}\,x^2 + 0.05671\,x + 5.0434\times10^{-4}$	0.9996	0.08	0.16~20.00
90	PGD1	$y = 0.21386\,x - 0.00515$	0.9999	0.16	0.31~5.00
91	PGD2	$y = 0.04722\,x + 0.01713$	0.9999	0.31	0.63~5.00
92	PGD3	$y = 1.3449\times10^{-4}\,x^2 + 0.03373\,x - 3.64892\times10^{-4}$	0.9997	0.31	0.63~5.00
93	PGE1	$y = 0.86363\,x + 0.01295$	0.9993	0.01	0.02~5.00
94	PGE3	$y = 0.16777\,x + 0.01071$	0.9997	0.08	0.16~5.00
95	PGF1α	$y = -0.04092\,x^2 + 0.65542\,x + 0.00814$	0.9996	0.04	0.08~5.00
96	PGF2α	$y = 0.17119\,x + 0.00811$	0.9991	0.08	0.16~20.00
97	PGF3α	$y = 0.13214\,x + 0.00486$	0.9946	0.08	0.16~5.00
98	PGJ2	$y = 0.07488\,x + 0.02526$	0.9993	0.31	0.63~20.00
99	tetranor-12S-HETE	$y = 0.01761\,x + 2.96056\times10^{-4}$	0.9999	0.08	0.16~20.00
100	TXB1	$y = -2.53606\times10^{-5}\,x^2 + 0.00633\,x + 1.94694\times10^{-4}$	0.9994	0.16	0.31~20.00
101	TXB2	$y = 0.1157\,x - 0.01421$	0.9992	0.04	0.08~5.00
102	TXB3	$y = -178.38621\,x^2 + 4.88545\times10^{4}\,x + 18432.76497$	0.9998	0.31	0.63~20.00
103	Δ17-6-keto PGF1α	$y = 0.00582\,x + 5.6582\times10^{-4}$	0.9994	0.63	1.25~20.00

Table S7 The accuracy and precision of quantitative 103 lipid mediators.

No.	Compounds	Concentration (ng/mL)	Accuracy (%)	Precision (RSD%)	No.	Compounds	Concentration (ng/mL)	Accuracy (%)	Precision (RSD%)	No.	Compounds	Concentration (ng/mL)	Accuracy (%)	Precision (RSD%)
1	±11(12)-EET	0.5	100.1	4.7	36	13,14-dihydro-15-keto PGD2	0.5	95.8	7.3	71	6S-LXA4	2.0	100.9	6.2
2	±11,12-DiHETrE	0.5	97.1	2.9	37	13,14-dihydro-15-keto PGF2α	2.0	104.9	6.2	72	6-trans LTB4	0.5	92.0	3.6
3	±11-HDoHE	2.0	110.6	3.5	38	13-OxoODE	2.0	93.5	7.2	73	8-iso PGF2α	2.0	102.6	7.0
4	±11-HEPE	2.0	109.6	2.9	39	13S-HODE	0.5	105.0	7.3	74	8-iso-15-keto PGF2β	0.5	96.2	6.5
5	±12(13)-DiHOME	0.5	95.6	5.6	40	13S-HOTrE	2.0	102.7	3.6	75	8S,15S-DiHETE	2.0	96.9	6.9
6	±12(13)-EpOME	2.0	108.5	5.0	41	13S-HOTrE(γ)	2.0	102.5	4.9	76	8S-HETrE	0.5	92.5	5.2
7	±13-HDoHE	0.5	95.4	7.7	42	14,15-LTC4	10.0	98.5	8.2	77	9-Nitrooleic Acid	0.5	108.8	9.4
8	±14(15)-EET	0.5	95.3	7.5	43	14,15-LTD4	2.0	99.2	5.5	78	9-OxoODE	2.0	95.5	8.2
9	±14(15)-EpETE	2.0	95.3	8.2	44	14,15-LTE4	2.0	93.3	6.1	79	9R-HETE	2.0	93.4	4.2
10	±14,15-DiHETrE	0.5	97.4	5.2	45	±11(12)-EET	0.5	100.1	4.7	80	9S-HODE	0.5	113.7	2.8
11	±16,17-EpDPE	2.0	106.4	5.4	46	15-deoxy-Δ12,14-PGD2	0.5	95.5	3.2	81	9S-HOTrE	0.5	95.2	5.5
12	±17(18)-EpETE	2.0	90.7	10.2	47	15-deoxy-Δ12,14-PGJ2	0.5	111.1	3.9	82	ARA	0.5	93.4	5.6
13	±18-HETE	2.0	112.4	3.6	48	15-keto PGE2	0.5	97.2	5.5	83	DHA	0.5	99.6	5.9
14	±19(20)-DiHDPA	2.0	94.5	3.4	49	15-keto PGF1α	0.5	93.1	8.0	84	DTA	0.5	97.9	7.7
15	±19,20-EpDPE	0.5	89.8	3.2	50	15-OxoEDE	2.0	112.3	3.5	85	EPA	0.5	101.4	6.6
16	±20-HDoHE	2.0	102.9	5.9	51	15-OxoETE	0.5	102.2	8.2	86	LTE4	2.0	101.1	4.6
17	±5,6-DiHETrE	0.5	101.6	6.0	52	15S-HEPE	2.0	109.3	4.0	87	LXA5	2.0	99.3	9.3
18	±5-iso PGF2α-VI	2.0	95.0	7.1	53	15S-HETrE	0.5	94.5	3.8	88	PGA2	0.5	104.3	4.8
19	±8(9)-EET	2.0	99.7	6.5	54	16S-HETE	0.5	95.1	5.5	89	PGB2	2.0	90.2	3.8
20	±8,9-DiHETrE	2.0	101.8	3.5	55	17S-HETE	0.5	103.2	5.7	90	PGD1	0.5	98.5	7.2
21	±8-HDoHE	0.5	94.4	7.2	56	19R-hydroxy PGE2	0.5	92.1	3.2	91	PGD2	0.5	98.9	5.5
22	±9(10)-DiHOME	2.0	92.0	4.2	57	19R-hydroxy PGF2α	0.5	92.2	2.5	92	PGD3	0.5	99.7	5.3
23	±9(10)-EpOME	0.5	101.5	4.4	58	19S-HETE	2.0	106.7	5.2	93	PGE1	0.5	110.7	2.0
24	10-Nitrooleic Acid	0.5	103.1	7.8	59	1a,1b-dihomo PGE2	0.5	96.0	4.4	94	PGE3	0.5	108.8	5.8
25	11-dehydro TXB2	0.5	97.7	7.2	60	1a,1b-dihomo PGF2α	0.5	98.9	7.0	95	PGF1α	0.5	89.0	2.8
26	11S-HETE	0.5	110.5	3.4	61	2,3-dinor TXB2	2.0	98.9	6.1	96	PGF2α	2.0	106.5	4.5
27	11β-13,14-dihydro-15-keto PGF2α	2.0	105.3	4.3	62	2,3-dinor-11β-PGF2α	2.0	91.2	4.2	97	PGF3α	0.5	100.1	4.5
28	11β-PGE2	0.5	93.9	4.8	63	2,3-dinor-8-iso-PGF2α	0.5	88.9	4.0	98	PGJ2	2.0	101.3	4.7
29	11β-PGF2α	2.0	90.2	6.7	64	20-carboxy LTB4	2.0	91.7	7.6	99	tetranor-12S-HETE	2.0	93.1	5.4
30	12-oxo LTB4	2.0	94.0	5.4	65	20-HETE	2.0	106.8	4.5	100	TXB1	2.0	99.9	6.8
31	12-OxoETE	0.5	102.8	7.1	66	20-hydroxy LTB4	2.0	87.4	7.0	10	TXB2	0.5	99.1	8.6
32	12S-HEPE	2.0	110.3	2.6	67	5-OxoETE	0.5	99.0	8.8	102	TXB3	2.0	97.0	4.2
33	12S-HETE	0.5	108.9	3.8	68	5S,6R-DiHETE	0.5	92.0	5.6	103	Δ17-6-keto PGF1α	2.0	102.2	6.4
34	12S-HHTrE	2.0	97.5	3.7	69	5S-HEPE	0.5	108.8	2.3					
35	13,14-dihydro PGF2α	2.0	104.5	5.3	70	5S-HETrE	0.5	91.0	9.9					

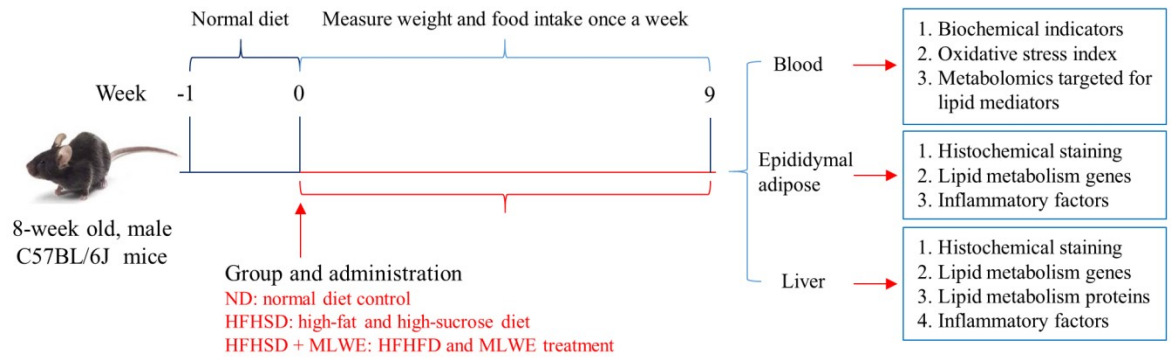


Figure S1 Experimental design. NC, HFHS, and HSML groups represent the normal diet control group treated with drug-free solution, high-fat and high-sugar diet group treated with drug-free solution, and HFHS group treated with MLWE, respectively.

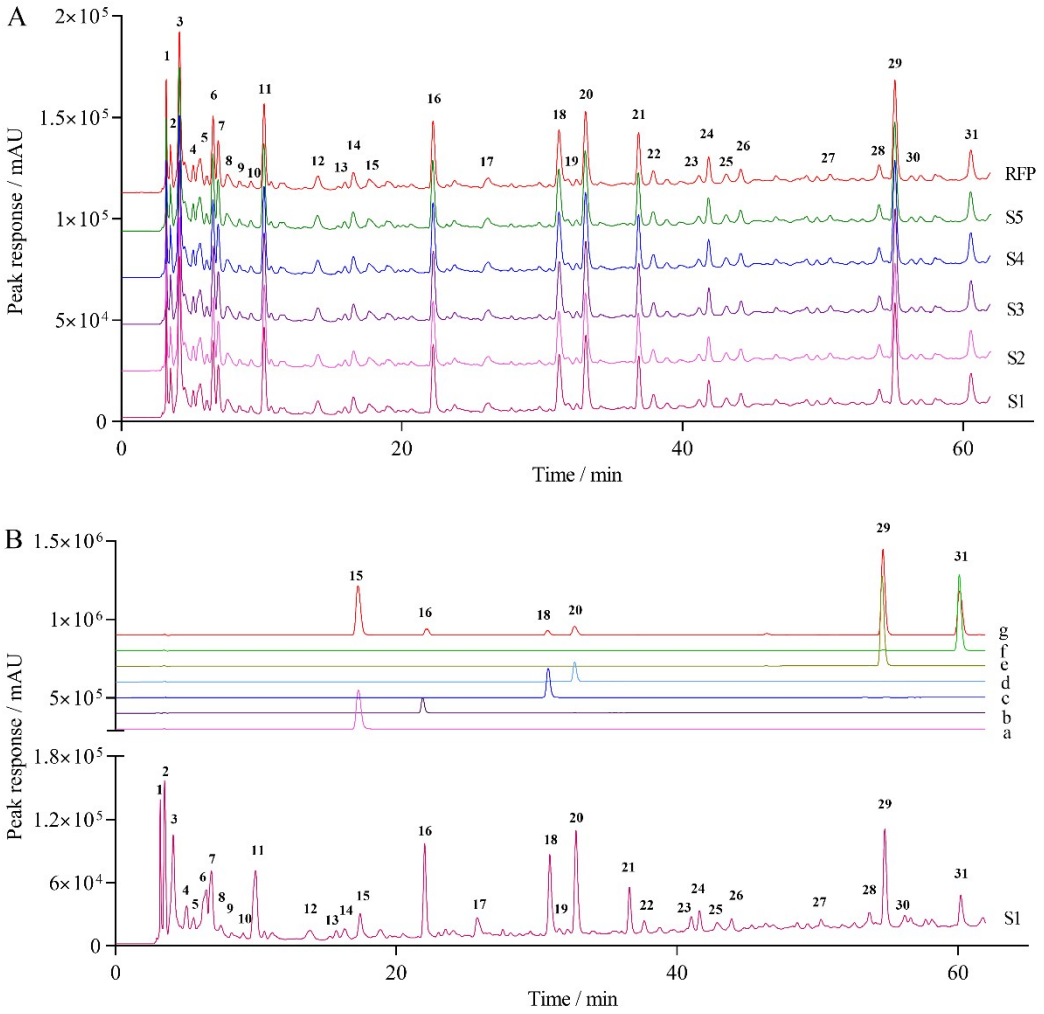
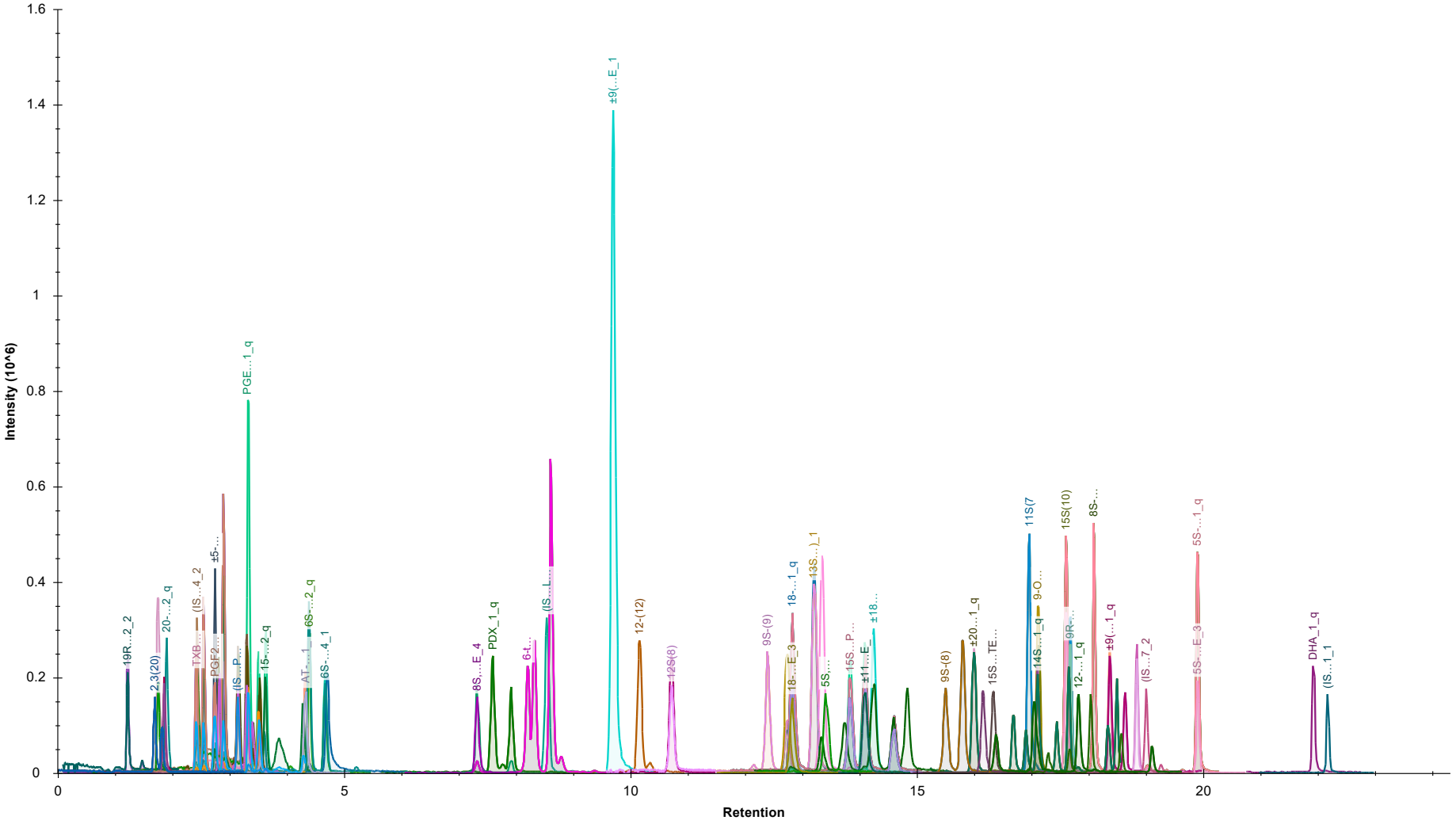


Figure S2 Representative HPLC chromatographic fingerprints (A) and characteristic peaks (B) of 5 batches of MLWE detected at 254 nm. MLWE represent mulberry leaves water extraction. RFP means reference fingerprint; S1~S5 mean 5 batches of MLWE prepared by different operators at different times, respectively; a, b, c, d, e, f, and g respectively represent protocatechuic acid, neochlorogenic acid, chlorogenic acid, cryptochlorogenic acid, rutin, astragalin and mixed standards.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Retention
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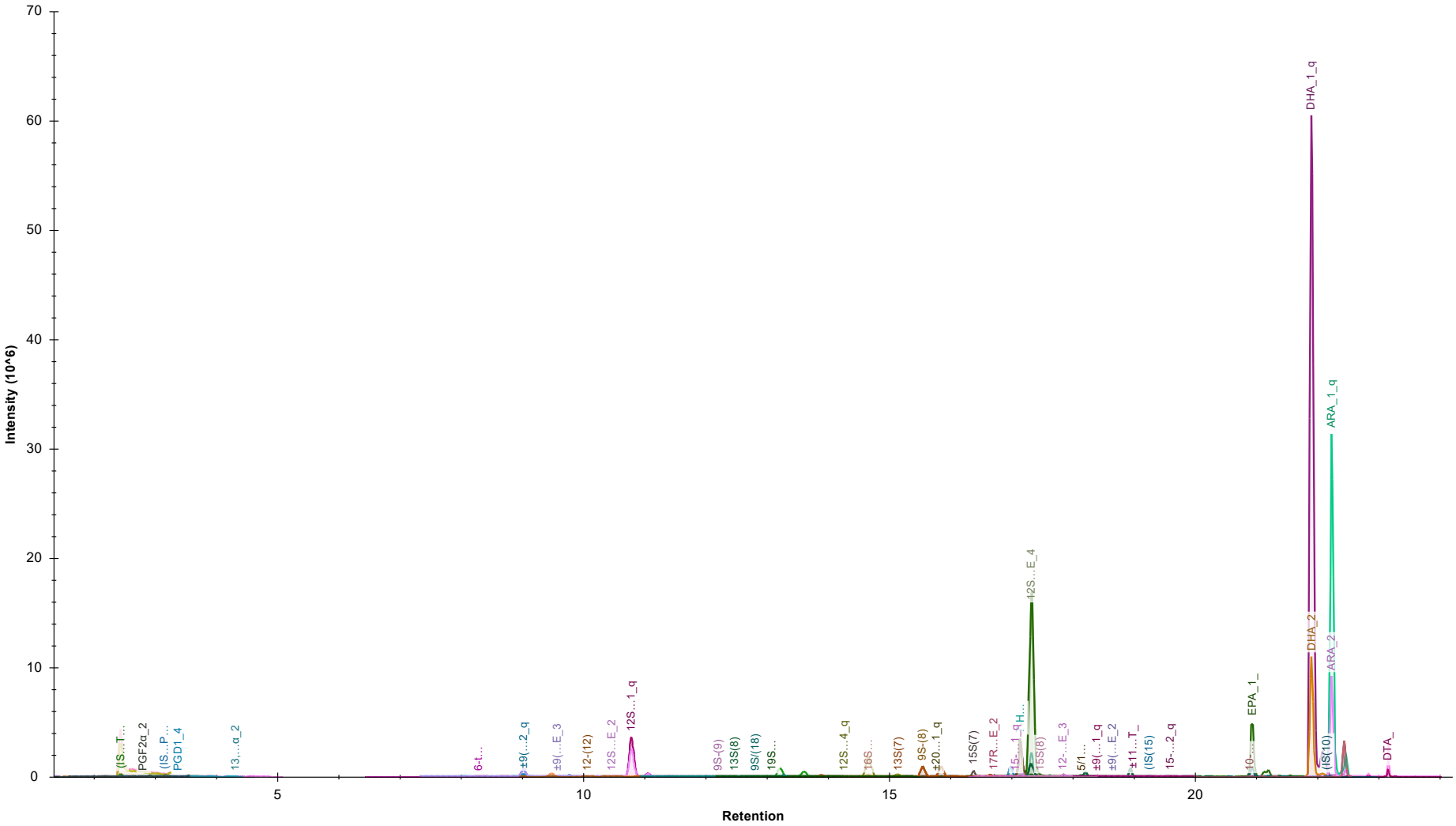
0.4
0.6
0.8
1
1.2
1.4
1.6
0
5
10
15
20
19R...2_2
2,3(20)
20-...2_q
TXB...
(IS...4_2
PGF2...
±5-...
(IS...P...
PGE...1_q
15-...2_q
AT...1
6S-...2_q
6S-...4_1
8S...E_4
PDX_1_q
6-t...
(IS...t...
±9(...E_1
12-(12)
12S(8)
9S-(9)
18-...1_q
18...E_3
13S...)_1
5S,...
15S...P...
±11...E_
±18...
9S-(8)
±20...1_q
15S...TE...
11S(7
14S...1_q
9-O...
15S(10)
9R-...
12-...1_q
8S-...
±9(...1_q
(IS...7_2
5S-...E_3
5S-...1_q
DHA_1_q
(IS...1_1


Intensity (10^6)
Retention
0
10
20
30
40
50
60
70
5
10
15
20
(IS...T...
PGF2α_2
(IS...P...
PGD1_4
13,...α_2
6-t...
±9(...2_q
±9(...E_3
12-(12)
12S...E_2
12S...1_q
9S-(9)
13S(8)
9S/(18)
19S...
12S...4_q
16S...
13S(7)
9S-(8)
±20...1_q
15S(7)
17R...E_2
12S...E_4
15S(8)
12-...E_3
5/1...
±9(...1_q
±9(...E_2
±11...T_
(IS(15)
15-...2_q
EPA_1_
DHA_1_q
DHA_2
(IS(10)
ARA_1_q
ARA_2
DTA_