

Table S1 Identification of individual compounds in LRE by UPLC-ESI-MS/MS.

Peak	RT (min)	Type	Compound identity	Formula	Molecular Weight	Intenisy
1	0.19	[M+H] ⁺	N-Butylbenzenesulfonamide	C ₁₂ H ₁₂ N ₂ O ₂	213.08	1172002.27
2	0.92	[M-H] ⁻	Galactonic acid	C ₆ H ₁₂ O ₇	196.06	85645350.66
3	0.97	[M+H] ⁺	Choline	C ₅ H ₁₃ NO	103.10	59348954.48
4	1.03	[M+H] ⁺	Leucine	C ₆ H ₁₃ NO ₂	131.09	9119821.89
5	1.09	[M-H] ⁻	trans-Aconitic acid	C ₆ H ₆ O ₆	174.02	21508474.64
6	1.09	[M+H] ⁺	Betaine	C ₅ H ₁₁ NO ₂	117.08	409020222.08
7	1.11	[M+H] ⁺	Trigonelline	C ₇ H ₇ NO ₂	137.05	9855025.46
8	1.19	[M+H] ⁺	Muramic acid	C ₉ H ₁₇ NO ₇	251.10	151044669.84
9	1.19	[M-H] ⁻	2-Hydroxynicotinic acid	C ₆ H ₅ NO ₃	139.03	2691149.56
10	1.21	[M+H] ⁺	Pipecolic acid	C ₆ H ₁₁ NO ₂	129.08	13199497.93
11	1.22	[M+H] ⁺	Pyridoxal	C ₈ H ₉ NO ₃	167.06	5264616.03
12	1.28	[M+H] ⁺	3-Hydroxy-2-methylpyridine	C ₆ H ₇ NO	109.05	5358662.57
13	1.30	[M+H] ⁺	6-Hydroxynicotinic acid	C ₆ H ₅ NO ₃	139.03	12527400.20
14	1.41	[M-H] ⁻	Citric acid	C ₆ H ₈ O ₇	192.03	670358791.44
15	1.42	[M+H] ⁺	L-Tyrosine	C ₉ H ₁₁ NO ₃	164.05	8880749.88
16	1.43	[M+H] ⁺	L-Pyroglutamic acid	C ₅ H ₇ NO ₃	129.04	9336644.04
17	1.57	[M+H] ⁺	L-Norleucine	C ₆ H ₁₃ NO ₂	131.09	21930931.34
18	2.02	[M+H] ⁺	Phenacetin	C ₁₀ H ₁₃ NO ₂	179.09	5919964.63
19	2.74	[M+H] ⁺	L-Phenylalanine	C ₉ H ₁₁ NO ₂	165.08	61439442.24
20	3.80	[M-H] ⁻	2,3-Dihydroxybenzoic acid	C ₇ H ₆ O ₄	154.03	1582508.72
21	4.05	[M+H] ⁺	Methyl isonicotinate	C ₇ H ₇ NO ₂	137.05	2673578.69
22	4.64	[M-H] ⁻	Neochlorogenic acid	C ₁₆ H ₁₈ O ₉	354.09	5555159.71
23	4.65	[M+H] ⁺	Ethyl levulinate	C ₇ H ₁₂ O ₃	144.08	470417.56
24	4.81	[M-H] ⁻	N-Acetylvaline	C ₇ H ₁₃ NO ₃	159.09	1070307.37
25	5.30	[M-H] ⁻	4-Acetyl-3-hydroxy-5-methylphenyl β-D-glucopyranoside	C ₁₅ H ₂₀ O ₈	328.12	965620.31
26	5.31	[M-H] ⁻	2-Isopropylmalic acid	C ₇ H ₁₂ O ₅	176.07	10114089.23
27	5.54	[M-H] ⁻	D-(-)-Quinic acid	C ₇ H ₁₂ O ₆	192.06	10194822.21
28	5.54	[M-H] ⁻	Chlorogenic acid	C ₁₆ H ₁₈ O ₉	354.09	87595284.86
29	5.62	[M+H] ⁺	2,3,4,9-Tetrahydro-1H-β-carboline-3-carboxylic acid	C ₁₂ H ₁₂ N ₂ O ₂	216.09	12494620.88
30	5.63	[M+H] ⁺	6-Methylquinoline	C ₁₀ H ₉ N	143.07	3417801.28
31	5.69	[M-H] ⁻	3-[2-(β-D-Glucopyranosyloxy)-4-methoxyphenyl]propanoic acid	C ₁₆ H ₂₂ O ₉	358.13	1262407.67
32	5.85	[M-H] ⁻	Caffeic acid	C ₉ H ₈ O ₄	180.04	3618589.32
33	5.99	[M-H] ⁻	4-Hydroxybenzaldehyde	C ₇ H ₆ O ₂	122.04	904384.78
34	6.23	[M-H] ⁻	2-Hydroxycaproic acid	C ₆ H ₁₂ O ₃	132.08	8134946.52
35	6.42	[M+H] ⁺	4-Hydroxyindole	C ₈ H ₇ NO	133.05	2430941.58
36	6.45	[M-H] ⁻	N-Acetyl-D-alloisoleucine	C ₈ H ₁₅ NO ₃	173.10	769401.69
37	6.54	[M+H] ⁺	Pindone	C ₁₄ H ₁₄ O ₃	230.09	3382586.26

38	6.72	[M+H] ⁺	Paracetamol	C ₈ H ₉ NO ₂	151.06	5537206.10
39	6.90	[M-H] ⁻	3-Coumaric acid	C ₉ H ₈ O ₃	164.05	15721221.35
40	6.91	[M-H] ⁻	(3R,5R)-1,3,5-Trihydroxy-4- {(2E)-3-(4-hydroxy-3-methoxyphenyl)-2-propenoyl}oxy;cyclohexanecarboxylic acid	C ₁₇ H ₂₀ O ₉	368.11	3075953.36
41	6.92	[M-H] ⁻	Naringin	C ₂₇ H ₃₂ O ₁₄	580.18	2620848.14
42	6.96	[M-H] ⁻	N-Acetyl-L-phenylalanine	C ₁₁ H ₁₃ NO ₃	207.09	9139138.35
43	7.00	[M-H] ⁻	3-Phenyllactic acid	C ₉ H ₁₀ O ₃	166.06	3497024.61
44	7.14	[M+H] ⁺	Quercetin	C ₁₅ H ₁₀ O ₇	302.04	915462.86
45	7.15	[M-H] ⁻	Rutin	C ₂₇ H ₃₀ O ₁₆	610.15	13744493.83
46	7.19	[M+H] ⁺	Scopoletin	C ₁₀ H ₈ O ₄	192.04	4463608.19
47	7.25	[M+H] ⁺	Naringenin	C ₁₅ H ₁₂ O ₅	272.07	4626324.65
48	7.26	[M-H] ⁻	7-Hydroxy-2-(4-hydroxyphenyl)-4-oxo-3,4-dihydro-2H-chromen-5-yl β-D-glucopyranoside	C ₂₁ H ₂₂ O ₁₀	434.12	2849532.61
49	7.31	[M+H] ⁺	2-Hydroxycinnamic acid	C ₉ H ₈ O ₃	164.05	2871914.60
50	7.46	[M-H] ⁻	N-Acetyl-DL-tryptophan	C ₁₃ H ₁₄ N ₂ O ₃	246.10	12910878.79
51	7.46	[M-H] ⁻	DL-Tryptophan	C ₁₁ H ₁₂ N ₂ O ₂	204.09	796522.38
52	7.50	[M+H] ⁺	N-Feruloyloctopamine	C ₁₈ H ₁₉ NO ₅	311.11	1890918.60
53	7.61	[M+H] ⁺	Kaempferol-3-O-β-glucopyranosyl-7-O-α-rhamnopyranoside	C ₂₇ H ₃₀ O ₁₅	594.16	4247917.64
54	7.67	[M+H] ⁺	Tiliroside	C ₃₀ H ₂₆ O ₁₃	594.14	54069.66
55	7.69	[M+H] ⁺	5,7-Dihydroxy-2-(4-hydroxy-3-methoxyphenyl)-4-oxo-4H-chromen-3-yl 6-O-(6-deoxy-α-L-mannopyranosyl) hexopyranoside	C ₂₈ H ₃₂ O ₁₆	624.17	2250284.46
56	8.24	[M-H] ⁻	Azelaic acid	C ₉ H ₁₆ O ₄	188.10	2487690.47
57	8.26	[M-H] ⁻	Salicylic acid	C ₇ H ₆ O ₃	138.03	8720660.40
58	8.28	[M-H] ⁻	6-O-(3,4-Dihydroxy-2-methylenebutanoyl)-1-O-[(2E)-3-phenyl-2-propenoyl]-β-D-glucopyranose	C ₂₀ H ₂₄ O ₁₀	424.14	1176381.33
59	8.52	[M+H] ⁺	Prunin	C ₂₁ H ₂₂ O ₁₀	434.12	1038964.74
60	8.61	[M+H] ⁺	Nootkatone	C ₁₅ H ₂₂ O	218.17	1048748.65
61	8.63	[M+H] ⁺	(2E)-3-(4-Hydroxyphenyl)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide	C ₁₇ H ₁₇ NO ₃	283.12	2297119.58

62	8.73	[M-H]-	2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4H-chromen-3-yl 6-deoxy-2-O- $\{6\text{-O-}[(2\text{E})\text{-3-(4-hydroxyphenyl)-2-propenoyl]}\text{-}\beta\text{-D-glucopyranosyl}\}\text{-}\alpha\text{-L-glucopyranoside}$	$\text{C}_{36}\text{H}_{36}\text{O}_{18}$	756.19	1151485.75
63	8.73	[M+H]+	4-Phenylbutyric acid	$\text{C}_{10}\text{H}_{12}\text{O}_2$	164.08	363670.67
64	8.95	[M+H]+	Butyl 4-aminobenzoate	$\text{C}_{11}\text{H}_{15}\text{NO}_2$	193.11	4287056.81
65	9.04	[M+H]+	Ambrosic acid	$\text{C}_{15}\text{H}_{20}\text{O}_4$	246.12	417597.54
66	9.13	[M+H]+	Indirubin	$\text{C}_{16}\text{H}_{10}\text{N}_2\text{O}_2$	262.07	1402842.20
67	9.50	[M+H]+	Zerumbone	$\text{C}_{15}\text{H}_{22}\text{O}$	218.17	1592275.72
68	9.76	[M+H]+	Dimethyl phthalate	$\text{C}_{10}\text{H}_{10}\text{O}_4$	194.06	1338595.49
69	9.76	[M+H]+	7-Hydroxycoumarin	$\text{C}_9\text{H}_6\text{O}_3$	162.03	5057359.75
70	9.81	[M+H]+	(4S,4aR)-4-[(3S)-3-Hydroxy-3-methylpent-4-enyl]-3,4a,8,8-tetramethyl-5,6,7,8a-tetrahydro-4H-naphthalen-1-one	$\text{C}_{20}\text{H}_{32}\text{O}_2$	304.24	548852.58
71	9.83	[M+H]+	Nootkatone	$\text{C}_{15}\text{H}_{22}\text{O}$	218.17	789678.72
72	9.95	[M+H]+	Kaempferol	$\text{C}_{15}\text{H}_{10}\text{O}_6$	286.05	840503.91
73	10.06	[M-H]-	Corchorifatty acid F	$\text{C}_{18}\text{H}_{32}\text{O}_5$	328.22	128069353.05
74	10.06	[M+H]+	9S,13R-12-Oxophytodienoic acid	$\text{C}_{18}\text{H}_{28}\text{O}_3$	292.20	29800861.90
75	10.06	[M+H]+	19-Nortestosterone	$\text{C}_{18}\text{H}_{26}\text{O}_2$	274.19	19637434.66
76	10.07	[M+H]+	Andrographolide	$\text{C}_{20}\text{H}_{30}\text{O}_5$	350.21	2917731.89
77	10.08	[M+H]+	Ageratriol	$\text{C}_{15}\text{H}_{24}\text{O}_3$	234.16	2512513.95
78	10.24	[M+H]+	3-(4-Methylbenzoyl)acrylic acid	$\text{C}_{11}\text{H}_{10}\text{O}_3$	190.06	1531644.60
79	10.51	[M-H]-	(15Z)-9,12,13-Trihydroxy-15-octadecenoic acid	$\text{C}_{18}\text{H}_{34}\text{O}_5$	330.24	149927018.10
80	10.51	[M+H]+	Sedanolid	$\text{C}_{12}\text{H}_{18}\text{O}_2$	194.13	4274829.45
81	10.51	[M+H]+	Methyl cinnamate	$\text{C}_{10}\text{H}_{10}\text{O}_2$	162.07	1288162.99
82	10.83	[M-H]-	Dodecanedioic acid	$\text{C}_{12}\text{H}_{22}\text{O}_4$	230.15	248371.67
83	11.03	[M+H]+	Ciprostene	$\text{C}_{22}\text{H}_{36}\text{O}_4$	346.25	747053.98
84	11.10	[M+H]+	(-)-Caryophyllene oxide	$\text{C}_{15}\text{H}_{24}\text{O}$	220.18	1841249.93
85	11.32	[M+H]+	N,N'-Dicyclohexylurea	$\text{C}_{13}\text{H}_{24}\text{N}_2\text{O}$	224.19	2552337.10
86	11.49	[M+H]+	Methyl palmitate	$\text{C}_{17}\text{H}_{34}\text{O}_2$	287.28	1316384.60
87	11.91	[M+H]+	Bis(methylbenzylidene)sorbitol	$\text{C}_{24}\text{H}_{30}\text{O}_6$	386.17	1861186.72
88	12.33	[M+H]+	2-Amino-1,3,4-octadecanetriol	$\text{C}_{18}\text{H}_{39}\text{NO}_3$	317.29	3283623.32
89	12.36	[M+H]+	9-Oxo-10(E),12(E)-octadecadienoic acid	$\text{C}_{18}\text{H}_{30}\text{O}_3$	294.22	3715265.11
90	12.82	[M+H]+	Bis(4-ethylbenzylidene)sorbitol	$\text{C}_{24}\text{H}_{30}\text{O}_6$	414.20	26545164.21
91	12.86	[M+H]+	4-Ethoxy ethylbenzoate	$\text{C}_{11}\text{H}_{14}\text{O}_3$	194.09	803784.93

92	13.34	[M-H]-	Prostaglandin F1 α	C ₂₀ H ₃₆ O ₅	356.26	172460.92
93	13.66	[M-H]-	Hexadecanedioic acid	C ₁₆ H ₃₀ O ₄	286.21	318572.79
94	13.72	[M+H]+	Cetrimonium	C ₁₉ H ₄₁ N	283.32	738105.57
95	13.92	[M-H]-	6:2 Fluorinated telomer sulfonate	C ₈ H ₅ F ₁₃ O ₃ S	427.97	2276406.08
96	14.19	[M-H]-	13(S)-HpOTrE	C ₁₈ H ₃₀ O ₄	292.20	3106783.99
97	14.34	[M+H]+	3,5-di-tert-Butyl-4-hydroxybenzaldehyde	C ₁₅ H ₂₂ O ₂	234.16	2229813.26
98	14.42	[M-H]-	(+/-)12(13)-DiHOME	C ₁₈ H ₃₄ O ₄	296.24	12493041.66
99	14.66	[M+H]+	Dipropylene glycol dibenzoate	C ₂₀ H ₂₂ O ₅	342.15	8445501.79
100	14.92	[M+H]+	9-Oxo-10(E),12(E)-octadecadienoic acid	C ₁₈ H ₃₀ O ₃	294.22	75613488.99
101	15.02	[M+H]+	α -Linolenoyl ethanolamide	C ₂₀ H ₃₅ NO ₂	321.27	1468547.95
102	16.55	[M-H]-	Ursolic acid	C ₃₀ H ₄₈ O ₃	456.36	1204337.93
103	16.59	[M+H]+	Palmitoyl ethanolamide	C ₁₈ H ₃₇ NO ₂	299.28	1580410.63
104	16.62	[M+H]+	Oleanolic acid	C ₃₀ H ₄₈ O ₃	438.35	3924280.18
105	16.70	[M+H]+	17 α -Methyl-androstan-3-hydroxyimine-17 β -ol	C ₂₀ H ₃₃ NO ₂	319.25	2065637.24
106	16.71	[M+H]+	α -Eleostearic acid	C ₁₈ H ₃₀ O ₂	278.22	70425472.16
107	16.87	[M-H]-	16-Hydroxyhexadecanoic acid	C ₁₆ H ₃₂ O ₃	272.24	69067631.93
108	16.87	[M+H]+	Oleoyl ethanolamide	C ₂₀ H ₃₉ NO ₂	325.30	2273427.29
109	17.20	[M-H]-	2,2'-Methylenebis(4-methyl-6-tert-butylphenol)	C ₂₃ H ₃₂ O ₂	340.24	2859745.84
110	17.28	[M+H]+	Hexadecanamide e	C ₁₆ H ₃₃ NO	255.26	8673998.64
111	17.53	[M+H]+	Oleamide	C ₁₈ H ₃₅ NO	281.27	17007471.60
112	17.56	[M+H]+	3-Methyl-5-(5,5,8a-trimethyl-2-methylene-7-oxodecahydro-1-naphthalenyl)pentyl acetate	C ₂₂ H ₃₆ O ₃	348.27	5744994.03
113	17.56	[M-H]-	Linoleic acid	C ₁₈ H ₃₂ O ₂	280.24	16739517.14
114	17.74	[M+H]+	Adrenic acid	C ₂₂ H ₃₆ O ₂	332.27	1425446.44
115	17.95	[M+H]+	11(Z),14(Z),17(Z)-Eicosatrienoic acid	C ₂₀ H ₃₄ O ₂	306.26	1072400.30
116	18.40	[M-H]-	Ethyl myristate	C ₁₆ H ₃₂ O ₂	256.24	10008186.49
117	18.62	[M+H]+	9(Z),11(E),13(E)-Octadecatrienoic Acid methyl ester	C ₁₉ H ₃₂ O ₂	292.24	2472141.21
118	18.66	[M-H]-	Oleic acid	C ₁₈ H ₃₄ O ₂	282.26	17422186.94
119	18.72	[M+H]+	Docosatrienoic acid	C ₂₂ H ₃₈ O ₂	334.29	5568871.12
120	18.93	[M+H]+	Stearamide	C ₁₈ H ₃₇ NO	283.29	13855874.45
121	19.69	[M+H]+	Ethyl oleate	C ₂₀ H ₃₈ O ₂	310.29	4326779.49
122	19.70	[M+H]+	Muscone	C ₁₆ H ₃₀ O	238.23	8079249.78
123	19.95	[M-H]-	Stearic acid	C ₁₈ H ₃₆ O ₂	284.27	2604083.99
124	20.72	[M+H]+	Erucamide	C ₂₂ H ₄₃ NO	320.31	325612273.98
125	22.24	[M+H]+	Docosanamide	C ₂₂ H ₄₅ NO	339.35	844072.84
126	24.82	[M-H]-	Myristyl sulfate	C ₁₄ H ₃₀ O ₄ S	294.19	65962142.20

127	26.26	[M-H]-	4-Dodecylbenzenesulfonic acid	C ₁₈ H ₃₀ O ₃ S	326.19	73523620.14
128	27.15	[M+H]+	1,3-Benzodioxolylbutanamine (BDB)	C ₁₁ H ₁₅ NO ₂	193.11	600530.48
129	27.44	[M+H]+	Arachidonoyl amide	C ₂₀ H ₃₃ NO	303.26	603483.07

Table S2 Primary antibodies information

Primary antibodies	Dilution ratio	Item number	Vendor	Species
ZO-1	1: 1000	ab96587	Abcam	Rabbit
Occludin	1: 2000	GB11149	Proteintech	Rabbit
Claudin-1	1: 1000	13050-1-AP	Proteintech	Rabbit
E-cadherin	1: 1000	ab231303	Abcam	Mouse
MLCK	1: 5000	ab76092	Abcam	Rabbit
p-MLCK	1: 1000	ab200809	Abcam	Rabbit
Claudin-3	1: 200	34-1700	Thermo Fisher	Rabbit
Claudin-7	1: 200	34-9100	Thermo Fisher	Rabbit
PPAR γ	1: 1000	16643-1-AP	Proteintech	Rabbit
iNOS	1:100	ab15323	Abcam	Rabbit
COX-2	1: 1000	GB11077-2	Servicebio	Rabbit
p-I κ B	1: 500	14220-1-AP	Proteintech	Rabbit
NF- κ B p65	1: 500	ab16502	Abcam	Rabbit
p-p65	1: 500	13346	CST	Mouse
p-STAT3	1: 1000	AP0070	Abclonal	Rabbit
Ly6G	1: 1000	GB11229	Servicebio	Rabbit
F4/80	1:100	ab15580	Abcam	Rabbit
CD4	1: 1000	GB11064	Servicebio	Rabbit
IFN- γ	1: 1000	MAB4851	R&D Systems	Mouse
TLR4	1: 1000	GB11519	Servicebio	Rabbit
c-JUN	1: 1000	ab40766	Abcam	Rabbit
Caspase-1	1: 200	ab1872	Abcam	Rabbit
IL-1 β	1: 100	ab9722	Abcam	Rabbit
p-ERK	1: 1000	ab201015	Abcam	Rabbit
p-p38	1: 1000	ab47363	Abcam	Rabbit

p-JNK	1: 1000	ab124956	Abcam	Rabbit
IL-17	1: 1000	GB11110	Servicebio	Rabbit
Foxp3	1: 1000	GB11093	Servicebio	Rabbit
ASC	1: 1000	67824	CST	Rabbit
NLRP3	1: 1000	15101	CST	Rabbit
β -actin	1: 3000	GB12001	Servicebio	Mouse

Table S3 Primers used in Quantitative RT- PCR (QRT-PCR).

Gene name	Forward primer 5'-3'	Reverse primer 5'-3'
Muc2	CGTCTGGTGGAAATGGTGGAG	GCACGGGCGTAGGAAGAAA
RELM β	CCTGTCTGCTGGGATGGTT	GTGGCAAGTATTCCATTCCG
β -actin	GTGACGTTGACATCCGTAAGA	GTAACAGTCCGCCTAGAAGCAC

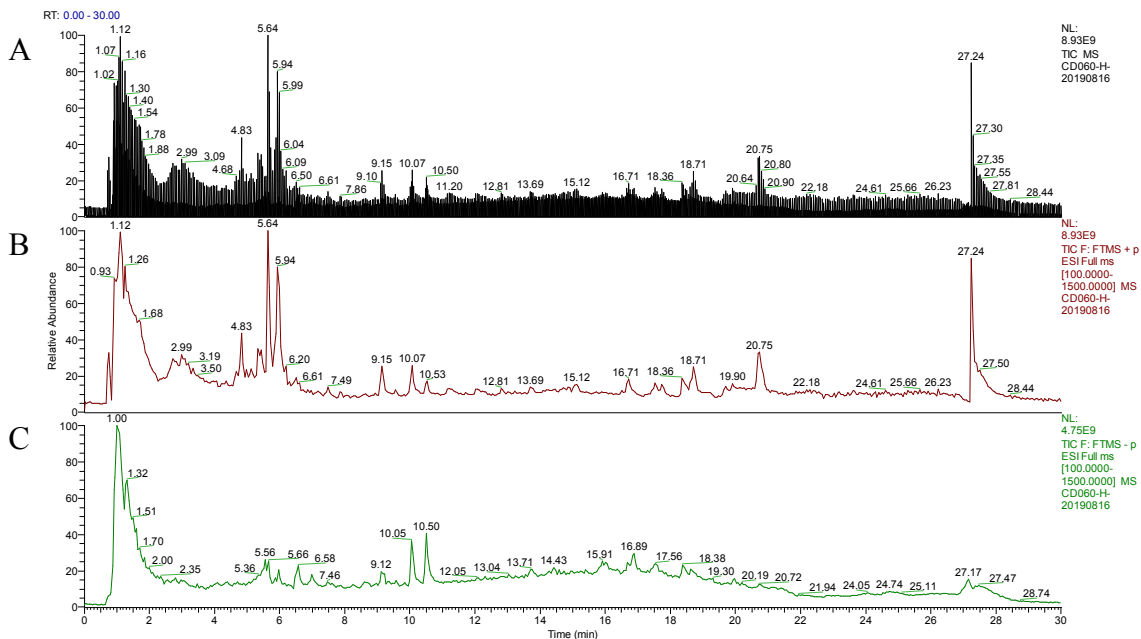


Figure S1. LC-ESI-MS/MS total ions chromatogram of LRE. (A) Total ions chromatogram, (B) positive ion mass spectrum, and (C) negative ion mass spectrum of LRE were displayed, respectively.