Supplementary data

Integrated Gas Chromatograph-Mass Spectrometry (GC/MS) and MS/MS-Based Molecular Networking Reveals the Analgesic and Anti-Inflammatory Phenotypes of the Sea Slater *Ligia exotica*

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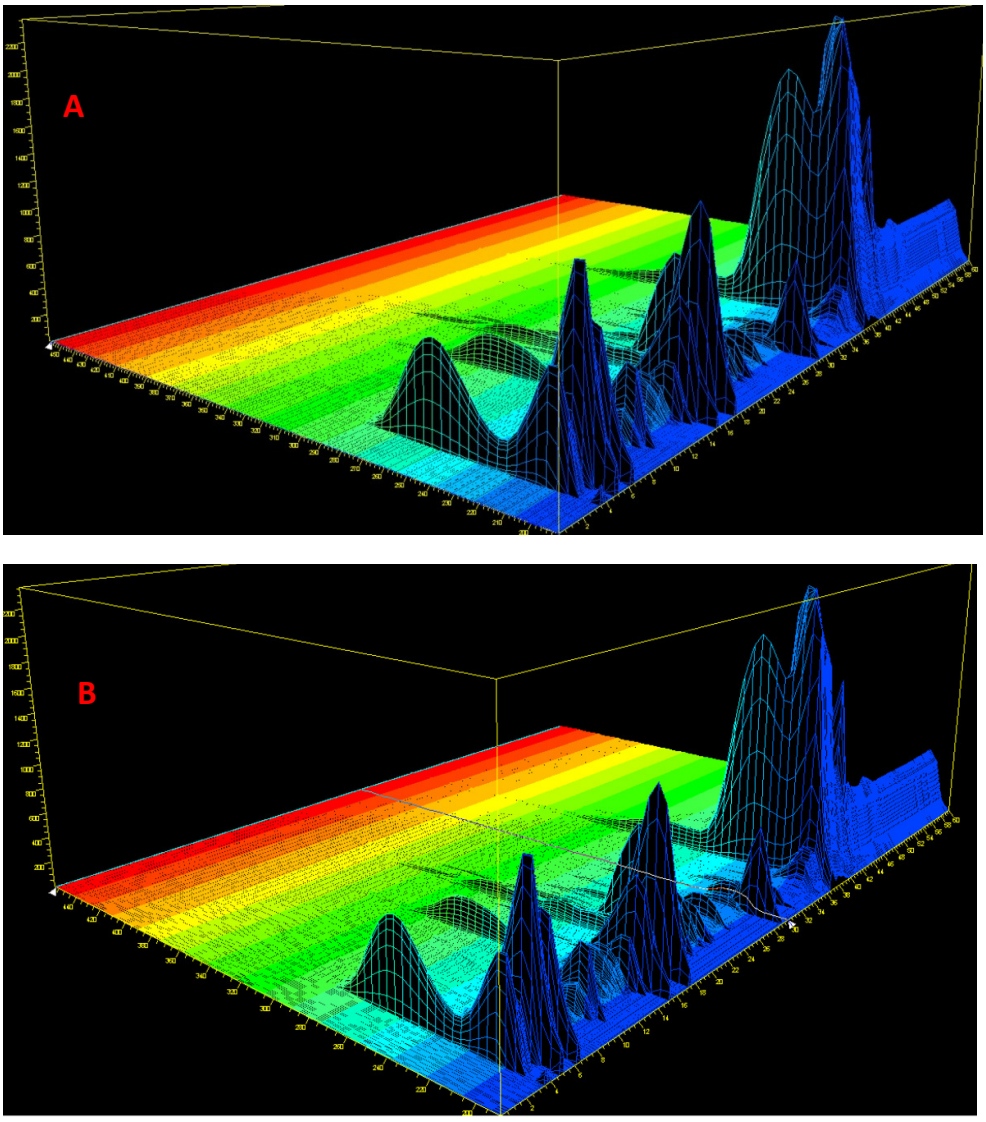
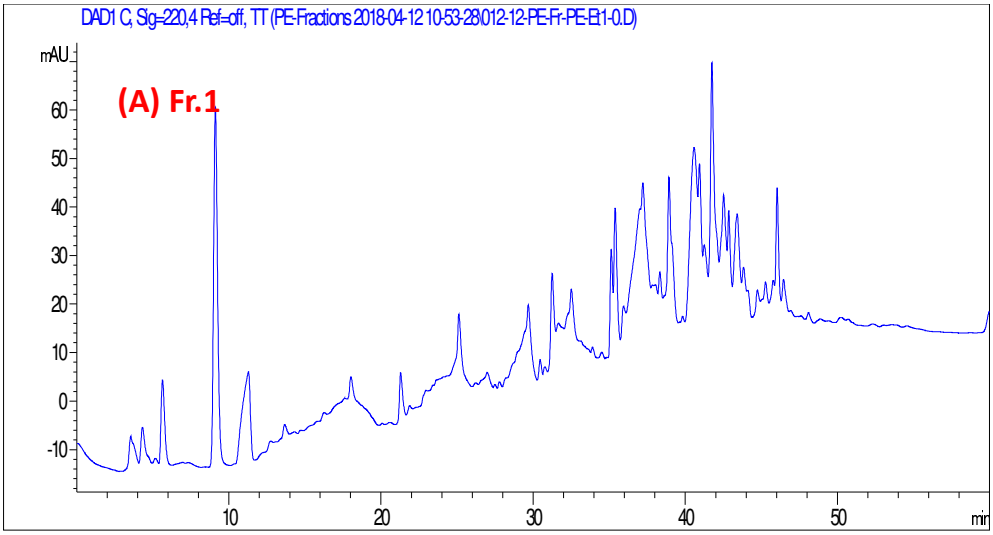


Figure S1. UV absorbance of peaks occurred in the HPLC chromatograms of PE (A) and EE (B) from 200 nm to 450 nm.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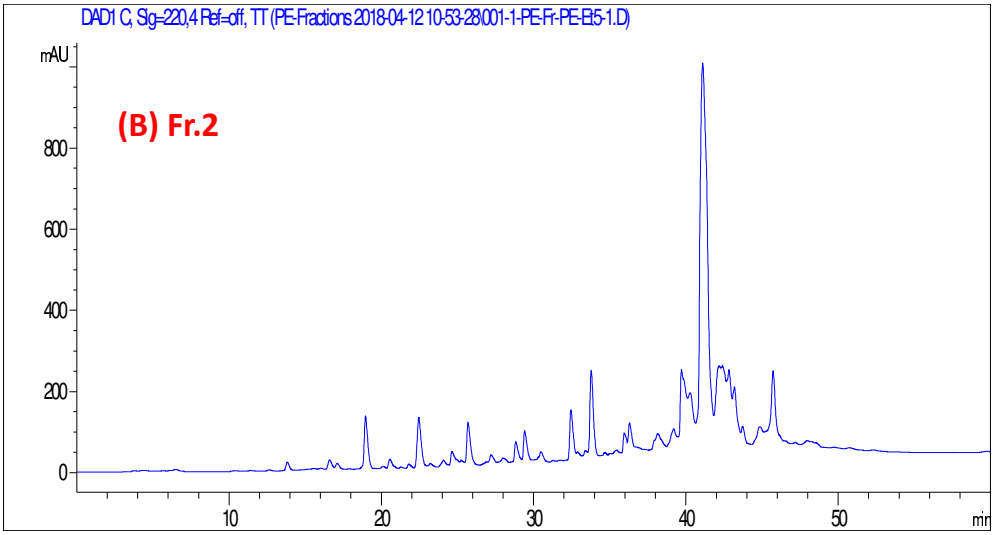
(A) Fr.1
mAU
60
50
40
30
20
10
0
-10
10
20
30
40
50
min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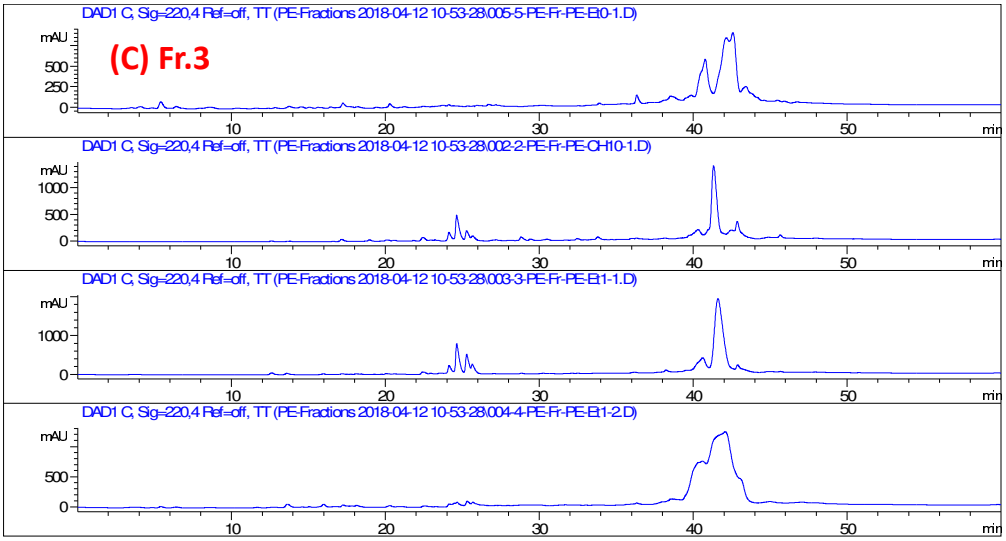
(B) Fr.2
mAU
800
600
400
200
0
10
20
30
40
50
min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(C) Fr.3
mAU
500
250
0
DAD1 C, Sig=220,4 Ref=off, TT (PE-Fractions 2018-04-12 10-53-28\002-2-PE-Fr-PE-CH10-1.D)
mAU
1000
500
0
DAD1 C, Sig=220,4 Ref=off, TT (PE-Fractions 2018-04-12 10-53-28\003-3-PE-Fr-PE-Et1-1.D)
mAU
1000
0
DAD1 C, Sig=220,4 Ref=off, TT (PE-Fractions 2018-04-12 10-53-28\004-4-PE-Fr-PE-Et1-2.D)
mAU
500
0
10
20
30
40
50
min

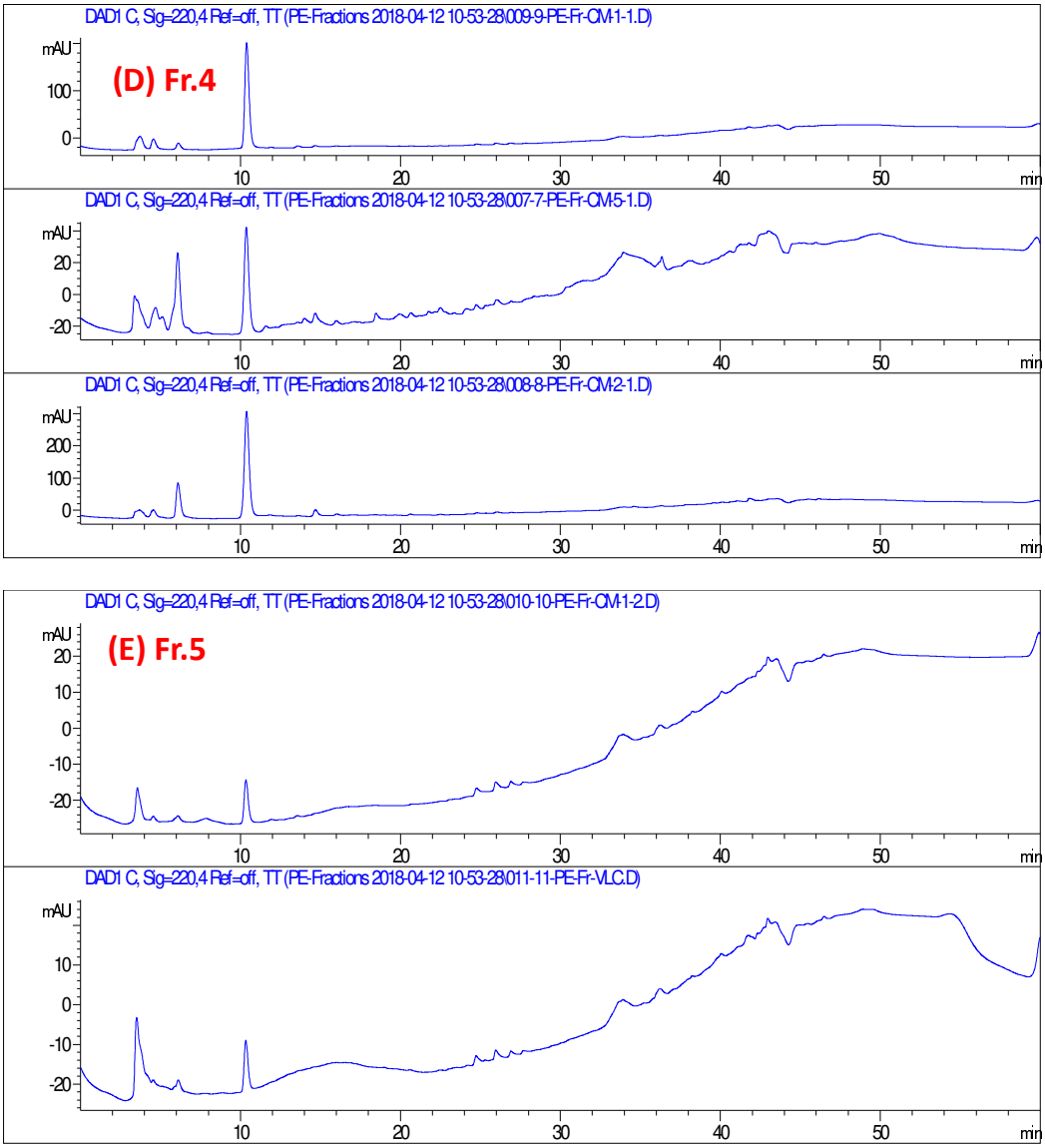

Figure S2. HPLC chromatograms of the combined PE fractions Fr.1-5 (A-E) at 220 nm.

Names	total	Compounds
50E 95E EE ME PE	2	19 43
95E EE ME PE	1	36
50E 95E ME PE	3	18 2 1
95E EE PE	1	42
95E ME PE	8	10 11 29 40 14 3 8 4
EE PE	18	33 7 26 27 20 31 12 15 45 30 25 28 24 22 46 23 13 34
ME PE	1	39
95E PE	1	6
95E ME	3	63 64 62
PE	11	32 21 16 44 35 41 17 9 38 37 5
EE	15	55 57 61 48 50 58 52 60 56 54 59 49 53 51 47
95E	3	65 66 67
50E	2	68 69

Figure S3. Outputs of venn diagram using the compounds 1-69 identified from PE, EE, ME, 95E, 50E by MS/MS-based spectral matching. The compound names have been shown in Table 5, and visualization of the results is presented in Figure 7A.

Table S1. The relative content of the major compounds identified from PE and EE by comparing their respective peak area to the total areas.

Compound_Names (MD[a] ≥ 95%)	**Relative Peak Area** (%)				
	PE-Fr.1	PE-Fr.2	PE-Fr.3	PE-Fr.4	EE
Z-9-hexadecenoic acid	-[d]	32.69	39.40	-	36.06
Z-11-hexadecenoic acid	29.86	-	-	-	-
n-hexadecanoic acid	-	1.85	5.34	-	3.20
Ethyl 9-hexadecenoate	5.3	0.38	1.84	-	-
(Z,Z)-9,12-octadecadienoic acid	3.98	7.81	-	-	3.44
E-13-octadecenoic acid	12.83	-	-	-	-
6-octadecenoic acid	9.00	23.62	32.88	-	1.95
Ethyl oleate	4.58	2.58	-	-	-
Cholesterol	6.52	17.12	-	-	-
Unsaturated fatty acids	55.67	65.97	77.62	-	44.65
SUM[b]	68.09	86.05	79.42	0	44.65
SUM[C]	79.99	89.60	80.13	0	56.31
Unidentified peaks	20.01	11.40	19.87	100	46.69

Notes: a, MD means Matching Degree; b, SUM represents the sum of relative peak area of the compounds listed in this table; c, SUM means the total sum of relative peak area of all compounds identified by GC-MS with MD ≥ 95%; d, not detected.

Table S2. Compounds putatively identified from *Logia* extracts by MS/MS spectral comparison with cosine score value of 0.70

Compounds	RT_Query(s)	Precursor_MZ(Da)	Compound_Name	SharedPeaks	MQScore
1	70.802	166.087	Massbank:PB000408 Phenylalanine|2-amino-3-phenylpropanoic acid	6	0.956563
	70.802	166.083	Spectral Match to DL-Phenylalanine from NIST14	17	0.926237
2	82.189	205.098	Massbank:PB006083 Tryptophan|(2S)-2-amino-3-(1H-indol-3-yl)propanoic acid	25	0.954918
	82.189	205.097	Spectral Match to L-Tryptophan from NIST14	30	0.952962
3	83.523	188.07	Spectral Match to Abrine from NIST14(3-(2-Indolyl)-2-methylaminopropanoic acid)	10	0.920207
4	83.523	188.071	Spectral Match to DL-Indole-3-lactic acid from NIST14	13	0.921548
5	96.254	265.154	Spectral Match to Phe-Val from NIST14	19	0.787928
6	127.29	231.114	1,2,3,4-tetrahydroharmane-3-carboxylic acid	10	0.85109
7	147.378	136.076	Spectral Match to DL-Octopamine from NIST14	6	0.728619
8	151.331	279.17	Spectral Match to Phe-Leu from NIST14	14	0.923904
9	171.655	279.169	Spectral Match to Leu-Phe from NIST14	7	0.718983
10	214.147	279.169	Spectral Match to Phe-Ile from NIST14	8	0.909698
11	260.648	208.097	NCGC00042134-05_C11H13NO3_N-Acetylphenylalanine	12	0.836929
	260.648	208.097	Spectral Match to L-Phenylalanine, N-acetyl- from NIST14	10	0.91052
12	287.152	245.128	NCGC00380633-02_C14H16N2O2_Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-3-(phenylmethyl)-	18	0.718626
13	287.152	245.128	NCGC00381359-01_C14H18N2O3_Phenylalanine, prolyl-	19	0.747031
14	292.27	313.155	Spectral Match to Phe-Phe from NIST14	9	0.95749
15	393.38	164.107	N-acetyl-2-phenylethylamine	7	0.8942

16	883.698	333.206	NCGC00385270-01_C20H28O4_5-[2-(3-Furyl)ethyl]-8-hydroxy-5,6,8a-trimethyl-3,4,4a,5,6,7,8,8a-octahydro-1-naphthalenecarboxylic acid	168	0.727051
17	883.698	333.206	NCGC00385272-01_C20H28O4_5-[2-(3-Furyl)ethyl]-8a-(hydroxymethyl)-5,6-dimethyl-3,4,4a,5,6,7,8,8a-octahydro-1-naphthalenecarboxylic acid	169	0.730714
18	1018.02	415.211	NCGC00347704-02_C24H32O7_2H-Oxireno[1,10a]phenanthro[3,2-b]furan-10(11bH)-one, 5,7-bis(acetyloxy)-3,3a,4,5,6,7,7a,7b,8,8a-decahydro-4,4,7a,11-tetramethyl-, (1aS,3aR,5S,7S,7aR,7bS,8aR,11bR)-	49	0.887886
19	1018.02	415.211	NCGC00385811-01!6-[3-[(3,4-dimethoxyphenyl)methyl]-4-methoxy-2-(methoxymethyl)butyl]-4-methoxy-1,3-benzodioxole	25	0.896878
20	1101.95	301.215	Spectral Match to 14(15)-EpETE from NIST14	147	0.808564
21	1135.87	293.211	Spectral Match to 9(S)-HpOTrE from NIST14	52	0.712923
22	1148.93	301.216	Spectral Match to 17(18)-EpETE from NIST14	127	0.809739
23	1148.93	301.216	Spectral Match to (.+/-.)-8-Hydroxy-5Z,9E,11Z,14Z,17Z-eicosapentaenoic acid from NIST14	134	0.814645
24	1170.15	303.231	Spectral Match to 11S-Hydroxy-5Z,8Z,12E,14Z-eicosatetraenoic acid from NIST14	150	0.852725
25	1170.15	303.231	Spectral Match to 15(S)-Hydroxy-(5Z,8Z,11Z,13E)-eicosatetraenoic acid from NIST14	150	0.865231
26	1172.17	279.231	Spectral Match to Pinolenic acid from NIST14	96	0.773502
27	1176.45	295.226	Spectral Match to 13-Keto-9Z,11E-octadecadienoic acid from NIST14	86	0.820771
28	1178.25	277.216	Spectral Match to 13S-Hydroxy-9Z,11E,15Z-octadecatrienoic acid from NIST14	68	0.76488
29	1188.09	482.36	Spectral Match to 1-Hexadecyl-sn-glycero-3-phosphocholine from NIST14	7	0.887771

30	1191.89	317.211	9-hydroxy-1,4a-dimethyl-7-propan-2-yl-2,3,4,9,10,10a-hexahydrophenanthrene-1-carboxylic acid	114	0.732695
31	1191.89	317.211	NCGC00380535-01_C20H28O3_12-Oxopimara-9(11),15-dien-18-oic acid	132	0.727094
32	1200.88	277.216	Spectral Match to 9,12-Octadecadiynoic Acid from NIST14	63	0.707527
33	1211.54	317.211	7-ethenyl-1,4a,7-trimethyl-6-oxo-2,3,4,8,8a,9,10,10a-octahydrophenanthrene-1-carboxylic acid	51	0.713914
34	1216.52	295.227	Spectral Match to 9-Oxo-10E,12Z-octadecadienoic acid from NIST14	97	0.798115
35	1222.44	303.232	Spectral Match to 8S-Hydroxy-5Z,9E,11Z,14Z-eicosatetraenoic acid from NIST14	90	0.75798
36	1227.3	279.159	Spectral Match to Dibutyl phthalate from NIST14	9	0.923685
37	1290.23	323.258	Eicosanoids_15-oxoEDE_C20H34O3	45	0.722368
	1290.23	323.258	Spectral Match to 15-OxoEDE from NIST14	54	0.727381
38	1293.26	323.258	NCGC00169469-03_C20H34O3_1-Naphthalenecarboxylic acid, decahydro-5-(5-hydroxy-3-methylpentyl)-1,4a-dimethyl-6-methylene-, (1R,4aS,5R,8aS)-	107	0.736152
39	1316.52	552.401	Spectral Match to 1-Arachidoyl-2-hydroxy-sn-glycero-3-phosphocholine from NIST14	15	0.854794
40	1318.46	510.391	Spectral Match to Lyso-PAF C-18 from NIST14	9	0.893974
35	1349.1	303.23	Spectral Match to 8-HETE from NIST14	56	0.746991
41	1370.87	307.263	Spectral Match to Linolenic acid ethyl ester from NIST14	64	0.809892
42	1389.49	402.301	(Z)-N-hexadec-9-enoyl-L-phenylalanine	17	0.878151
43	1408.8	282.279	Spectral Match to 9-Octadecenamide, (Z)- from NIST14	37	0.795687
44	1463.23	404.316	NCGC00380823-01!2-(14-methylpentadecanoylamino)-3-phenylpropanoic acid	26	0.90229
45	1866.48	369.351	Spectral Match to Cholestan-3-one, (5.alpha.)- from NIST14	27	0.75334

46	1866.48	369.352	Spectral Match to Cholesterol from NIST14	24	0.763294
47	89.587	261.123	NCGC00384639-01_C14H16N2O3_Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-3-[(4-hydroxyphenyl)methyl]-	53	0.734621
48	115.327	180.102	N-acetyltyramine	9	0.811762
49	334.623	197.117	Loliolide	38	0.765238
	334.623	197.117	NCGC00385365-01_C11H16O3_2(4H)-Benzofuranone, 5,6,7,7a-tetrahydro-6-hydroxy-4,4,7a-trimethyl-, (6S,7aR)-	60	0.790237
50	354.718	146.06	Spectral Match to 1H-Indole-4-carboxaldehyde from NIST14	6	0.84395
51	356.703	284.139	cyclo(D-Trp-L-Pro)	16	0.950215
	356.703	284.139	NCGC00169940-02!3-(1H-indol-3-ylmethyl)-2,3,6,7,8,8a-hexahydropyrrolo[1,2-a]pyrazine-1,4-dione	17	0.933498
52	629.326	261.159	cyclo(Phe-Leu)	34	0.737895
53	662.681	334.155	NCGC00347762-02!3-benzyl-6-(1H-indol-3-ylmethyl)piperazine-2,5-dione	13	0.888409
54	684.967	295.129	Massbank:EA277006 Aspartame|3-amino-4-[(1-benzyl-2-keto-2-methoxy-ethyl)amino]-4-keto-butyric acid	11	0.751393
	684.967	295.129	Massbank:EA277012 Aspartame|3-amino-4-[(1-benzyl-2-keto-2-methoxy-ethyl)amino]-4-keto-butyric acid	14	0.750524
55	970.585	321.242	5-(1,2,4a,5-tetramethyl-7-oxo-3,4,8,8a-tetrahydro-2H-naphthalen-1-yl)-3-methylpentanoic acid	143	0.800957
	970.585	321.242	NCGC00180747-02!5-[(1S,2R,4aR)-1,2,4a,5-tetramethyl-7-oxo-3,4,8,8a-tetrahydro-2H-naphthalen-1-yl]-3-methylpentanoic acid	152	0.804541
56	1187.73	327.231	Spectral Match to (.+/-.)-11-Hydroxy-4Z,7Z,9E,13Z,16Z,19Z-docosahexaenoic acid from NIST14	82	0.733423
57	1187.73	327.23	Spectral Match to 19(20)-EpDPE from NIST14	80	0.725253

58	1261.82	297.242	Spectral Match to 9(10)-EpOME from NIST14	36	0.702697
59	1322.28	304.26	Spectral Match to Arachidonoyl amide from NIST14	74	0.857892
60	1471.59	358.31	phenylethylamide 357	46	0.81775
61	1551.27	628.187	NCGC00385199-01!2-[3,4-bis[[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy]phenyl]-5,7-dihydroxychromen-4-one	28	0.741822
62	132.068	263.138	Spectral Match to Phe-Pro from NIST14	14	0.772827
63	386.204	352.165	Spectral Match to Phe-Trp from NIST14	9	0.880003
64	506.815	352.165	Spectral Match to Trp-Phe from NIST14	9	0.815122
65	75.058	229.16	Spectral Match to Leu-Pro from NIST14	6	0.792858
66	200.695	332.218	Spectral Match to Thr-Val-Leu from NIST14	7	0.732416
67	207.742	277.119	Spectral Match to PyroGlu-Phe from NIST14	16	0.73009
68	62.857	182.081	Spectral Match to L-Tyrosine from NIST14	11	0.947038
69	99.71	295.128	Spectral Match to Glu Phe from METLIN	9	0.777446