

Support information

Table S1 Information of MS peaks identified.

Time (min)	Average Mz	Mz Types	Metabolite	Class	Intensity			
					CK	Low	Middle	High
0.668	146.1652	[M+H] ⁺	Spermidine ^a	Alkaloids	1.11E+03	3.87E+02*	1.23E+03	9.17E+02
0.729	191.0194	[M-H] ⁻	Citric acid ^a	Organic acids	1.16E+06	1.30E+06*	1.05E+06*	1.19E+06
0.740	166.9731	[M-H] ⁻	Phosphoenolpyruvic acid	Organic acids	6.59E+04	6.69E+04	8.70E+04*	9.02E+04*
0.744	131.1282	[M+H] ⁺	Agmatine	Others	1.13E+03	1.29E+03	1.28E+03	9.34E+02*
0.761	133.0151	[M-H] ⁻	Malic acid ^a	Organic acids	5.98E+05	5.82E+05	7.14E+05*	6.50E+05*
0.761	96.9609	[M-H] ⁻	Phosphoric acid	Others	1.70E+07	1.37E+07*	1.59E+07*	1.58E+07*
0.770	185.0098	[M-H] ⁻	2-Phosphoglycerate ^a	Others	2.77E+04	3.10E+04*	3.48E+04*	3.22E+04
0.783	259.0214	[M-H] ⁻	D-Glucose 6-phosphate ^a	Sugars	1.40E+05	1.64E+05*	1.59E+05*	1.48E+05*
0.787	117.0189	[M-H] ⁻	Succinic acid ^a	Organic acids	1.20E+04	1.15E+04	9.11E+03*	1.09E+04
0.792	147.0299	[M-H] ⁻	Citramalic acid	Organic acids	4.16E+03	4.62E+03*	3.26E+03*	4.79E+03*
0.796	132.0308	[M-H] ⁻	Aspartate ^a	Amino acids	3.14E+04	3.12E+04	3.41E+04*	2.74E+04*
0.797	188.0554	[M-H] ⁻	N-acetyl-DL-glutamic acid	Amino acids	2.07E+03	1.59E+03*	1.39E+03*	1.70E+03*
0.799	191.0553	[M-H] ⁻	Quinic acid ^a	Organic acids	5.63E+05	7.87E+05*	9.95E+05*	8.95E+05*
0.810	565.0465	[M-H] ⁻	Uridine 5'-diphospho-D-glucose ^a	Nucleosides	1.13E+04	1.21E+04	1.16E+04	1.24E+04*
0.831	175.1173	[M+H] ⁺	Arginine ^a	Amino acids	8.98E+02	1.58E+03*	1.40E+03*	1.35E+03*
0.860	131.0460	[M-H] ⁻	Methylsuccinic acid ^a	Organic acids	4.57E+03	3.09E+03*	1.58E+03*	2.94E+03*
0.861	104.1058	[M] ⁺	Choline ^a	Nucleosides	7.91E+04	7.82E+04	7.05E+04*	7.21E+04

0.861	104.07 22	[M+H] +	N,N-dimethylglycine	Amino acids	7.69 E+04	7.09E +04	6.74E +04*	6.73E +04*
0.886	130.04 75	[M+H] +	L-5-oxoproline ^a	Amino acids	3.66 E+04	3.79E +04	3.42E +04	2.54E +04*
0.893	148.05 86	[M+H] +	Glutamic acid ^a	Amino acids	3.38 E+03	3.46E +03	3.29E +03	2.82E +03*
0.901	156.07 39	[M+H] +	Histidine ^a	Amino acids	1.40 E+03	1.27E +03	1.82E +03*	1.60E +03
0.964	138.05 39	[M+H] +	Trigonelline ^a	Alkaloi ds	3.53 E+04	2.82E +04*	3.16E +04	2.90E +04*
0.976	116.07 00	[M+H] +	Proline ^a	Amino acids	1.87 E+04	1.75E +04	2.25E +04*	2.40E +04*
0.990	203.14 90	[M+H] +	N,N-dimethylarginine	Amino acids	1.93 E+03	1.42E +03	1.16E +03*	1.86E +03
0.994	527.15 55	[M+NH 4] ⁺	Melezitose ^a	Sugars	3.10 E+04	3.59E +04*	3.52E +04*	3.02E +04
0.995	365.10 16	[M+Na] +	Melibiose ^a	Sugars	9.67 E+03	1.35E +04*	1.19E +04*	1.07E +04
0.995	162.07 63	[M+H] +	N-methyl-L-glutamic acid	Amino acids	7.74 E+02	7.45E +02	5.21E +02	4.94E +02*
1.054	118.08 68	[M+H] +	Betaine ^a	Alkaloi ds	1.87 E+04	1.74E +04*	2.07E +04*	1.91E +04
1.188	152.05 63	[M+H] +	Guanine ^a	Nucleos ides	4.80 E+02	7.75E +02*	5.50E +02	4.81E +02
1.415	123.05 50	[M+H] +	Niacinamide ^a	Alkaloi ds	2.72 E+04	2.85E +04*	2.55E +04	2.03E +04*
1.539	113.03 39	[M+H] +	Uracil ^a	Nucleos ides	3.95 E+02	1.52E +03*	6.72E +02	3.10E +02
1.589	348.06 85	[M+H] +	AMP ^a	Nucleos ides	5.95 E+04	5.73E +04	6.78E +04*	6.29E +04
1.683	308.08 92	[M+H] +	Glutathione ^a	Amino acids	8.95 E+03	1.48E +04*	1.13E +04*	1.30E +04*
1.755	123.05 51	[M+H] +	Nicotinamide ^a	Alkaloi ds	2.74 E+04	2.73E +04	2.40E +04	1.93E +04*
1.862	180.06 79	[M-H] ⁻	Tyrosine ^a	Amino acids	4.01 E+04	4.05E +04	4.46E +04*	4.33E +04
2.060	104.04 55	[M+H] +	Biuret	Others	5.22 E+02	2.55E +02*	5.78E +02	3.52E +02*
2.069	664.11 20	[M+H] +	NAD ⁺ ^a	Nucleos ides	2.78 E+03	5.53E +03*	2.27E +03	2.76E +03
2.102	132.10 00	[M+H] +	Isoleucine ^a	Amino acids	9.84 E+03	8.85E +03	8.59E +03*	8.69E +03

2.746	250.07 14	[M-H]-	Phenylacetylaspatic acid	Amino acids	8.36 E+02	1.59E +03	1.15E +03*	6.87E +02*
6.138	182.04 34	[M-H]-	4-Pyridoxic acid	Vitamin s	3.40 E+04	3.27E +04	3.04E +04	2.66E +04*
6.461	220.11 74	[M+H] +	Pantothenic acid ^a	Vitamin s	6.70 E+02	6.63E +02	8.50E +02*	7.27E +02
6.646	312.12 56	[M+H] +	N2,N2-dimethylguanosine	Nucleos ides	1.63 E+03	1.72E +03	1.88E +03	1.22E +03*
6.994	367.10 13	[M-H]-	3-Feruloylquinic Acid	Phenoli c acids	4.18 E+05	4.89E +05*	3.69E +05	3.38E +05*
7.112	205.09 48	[M-H]-	Tryptophan ^a	Amino acids	3.61 E+04	2.98E +04	3.23E +04	3.01E +04*
7.649	138.05 48	[M+H] +	3-Aminobenzoic acid	Organic acids	3.32 E+04	5.99E +04*	4.19E +04*	7.28E +04*
7.689	339.10 56	[M+2K -H] ⁺	3-O-coumaroylquinic Acid	Phenoli c acids	7.96 E+03	9.90E +03	1.03E +04*	9.73E +03
7.729	153.01 99	[M-H]-	2,5-Dihydroxybenzoic acid	Organic acids	4.79 E+05	4.77E +05	4.62E +05	4.48E +05*
7.743	291.08 84	[M+H] +	Epicatechin ^a	Flavono ids	1.97 E+04	2.38E +04*	1.68E +04	1.99E +04
8.268	307.17 58	[M+H] +	Feruloyl agmatine	Phenoli c acids	1.24 E+03	3.22E +03*	3.99E +02*	5.53E +02*
8.448	377.14 48	[M+H] +	Riboflavin ^a	Vitamin s	1.59 E+03	2.21E +03*	1.33E +03	1.27E +03
8.624	121.03 02	[M-H]-	4-Hydroxybenzaldehyde	Others	6.79 E+04	7.01E +04	8.13E +04*	6.85E +04
8.666	595.16 59	[M+H] +	Biotin	Flavono ids	7.64 E+04	7.46E +04	5.60E +04*	6.22E +04*
8.704	609.16 68	[M-H]-	Hesperetin 7-O-Rutinoside	Flavono ids	1.55 E+06	1.35E +06*	1.21E +06*	1.23E +06
8.745	563.14 25	[M-H]-	Corymboside	Flavono ids	7.11 E+06	6.83E +06	6.45E +06	6.35E +06*
8.845	449.10 79	[M+H] +	homoorientin ^a	Flavono ids	7.43 E+05	7.37E +05	7.10E +05	6.02E +05*
8.902	449.10 36	[M+H] +	Isoorientin ^a	Flavono ids	6.82 E+05	7.30E +05	6.88E +05	6.08E +05*
8.907	565.15 61	[M+H] +	Schaftoside	Flavono ids	2.29 E+06	2.55E +06	2.23E +06	2.12E +06*
8.947	207.01 16	[M-H]-	2-Naphthalenesulfonic acid	Organic acids	1.84 E+02	2.07E +02	1.52E +02	1.48E +02*
9.085	447.09 56	[M-H]-	Luteolin 6-C-glucoside	Flavono ids	7.99 E+05	5.77E +05	7.17E +05*	6.15E +05*

9.157	433.10 48	[M+H] +	Isovitexin	Flavono ids	2.32 E+04	2.78E +04*	2.30E +04	2.68E +04
9.286	625.17 59	[M+H] +	Iscopalin 2-O- glucoside	Flavono ids	6.16 E+06	6.49E +06	5.30E +06*	5.54E +06*
9.320	579.17 32	[M+H] +	Vitexin 2-O- rhamnoside	Flavono ids	1.29 E+04	1.70E +04*	1.20E +04	1.55E +04
9.734	479.12 27	[M+H] +	Isorhamnetin 3-O- glucoside	Flavono ids	3.01 E+05	3.23E +05	2.53E +05	2.27E +05*
9.874	491.11 59	[M-H]-	Tricin 5-glucoside	Flavono ids	4.15 E+06	3.76E +06	3.59E +06	3.56E +06*
9.925	463.11 79	[M+H] +	Hispidulin 4-glucoside	Flavono ids	6.14 E+05	5.83E +05	8.23E +05*	4.78E +05*
10.01 7	579.16 63	[M+H] +	Apigenin 7-O- neohesperidoside	Flavono ids	9.77 E+04	8.05E +04	6.04E +04*	7.11E +04*
10.15 5	721.21 23	[M+FA -H]-	Icariin	Flavono ids	1.05 E+05	8.30E +04*	6.61E +04*	9.28E +04
10.29 0	431.09 78	[M-H]-	Genistin ^a	Flavono ids	3.73 E+04	3.31E +04	2.73E +04*	2.97E +04*
10.30 7	639.19 21	[M+H] +	Demethoxycentaureidi n 7-O-rutinoside	Flavono ids	6.28 E+06	7.28E +06*	5.80E +06*	6.47E +06
10.49 7	144.04 60	[M-H]-	Indole-3- carboxaldehyde ^a	Others	1.02 E+04	1.19E +04	1.07E +04	9.07E +03*
10.54 9	757.20 97	[M]+	Cyanidin 3-(2G- glucosylrutinoside)	Flavono ids	7.59 E+04	7.10E +04	6.64E +04*	5.62E +04*
10.63 6	463.12 09	[M]+	Peonidin 3-O- glucoside	Flavono ids	4.90 E+05	4.13E +05*	3.60E +05*	3.83E +05*
10.72 6	515.15 21	[M+H] +	Globularin	Others	2.92 E+05	2.85E +05	2.63E +05*	3.00E +05
11.53 6	314.13 67	[M+H] +	feruloyltyramine	Phenoli c acids	1.74 E+04	1.20E +04*	1.30E +04*	1.44E +04*
11.75 8	257.07 94	[M+H] +	Glycyrrhizin	Flavono ids	4.58 E+03	4.89E +03	5.08E +03	5.76E +03*
13.05 5	331.08 17	[M+H] +	Tricin	Flavono ids	1.01 E+06	1.26E +06*	8.49E +05*	1.27E +06*
16.77 8	483.26 26	[M-H]-	LPG 16:0	Lipids	1.41 E+05	1.24E +05	1.77E +05*	1.20E +05
17.16 0	308.22 18	[M+H] +	Dihydrocapsaicin	Others	3.40 E+03	3.50E +03	3.57E +03	3.87E +03*
17.18 0	325.18 45	[M-H]-	Hydroquinidine	Others	1.81 E+05	2.09E +05	1.92E +05	2.32E +05*
17.65 8	478.29 07	[M+H] +	LPE 18:2	Lipids	1.58 E+05	1.58E +05	1.99E +05*	1.50E +05

17.99 1	415.20 55	[M- H ₂ O+H] ⁺	Gelomulide N	Others	3.94 E+02	7.18E +02*	7.59E +02*	7.17E +02
18.56 8	454.29 11	[M+H] +	LPE 16:0	Lipids	9.60 E+04	1.12E +05*	1.09E +05*	9.69E +04
19.10 0	480.30 62	[M-H]-	LPE 18:1	Lipids	7.33 E+03	8.97E +03*	1.14E +04*	7.90E +03*
19.21 3	522.35 42	[M+H] +	LPC 18:1	Lipids	9.81 E+04	1.20E +05*	1.47E +05*	1.03E +05
19.26 4	247.16 35	[M-H]-	FA 16:4	Lipids	3.08 E+04	3.45E +04*	3.50E +04*	3.24E +04
19.53 0	468.31 01	[M+H] +	LPE 17:0	Lipids	2.67 E+03	3.48E +03	3.32E +03*	3.49E +03*
20.06 7	510.35 86	[M+H] +	LPC 17:0	Lipids	3.52 E+04	3.59E +04	4.63E +04*	3.93E +04
21.56 9	277.21 96	[M+H] +	FA 18:3 (Linolenic acid) ^a	Lipids	8.76 E+03	1.25E +04*	1.20E +04*	1.15E +04*
21.64 0	267.22 05	[M-H]-	FA 17:1	Lipids	3.03 E+03	2.66E +03	2.98E +03	4.03E +03*
22.03 9	728.52 50	[M-H]-	PE (O-18:0/18:2)	Lipids	4.12 E+03	3.62E +03	2.43E +03*	3.51E +03
22.27 3	301.21 13	[M-H]-	FA 20:5	Lipids	3.47 E+03	1.95E +03*	1.19E +04*	1.56E +04*
22.68 0	855.49 13	[M-H]-	PI (18:2/18:3)	Lipids	1.26 E+05	1.42E +05*	1.59E +05*	1.50E +05
22.75 4	765.44 63	[M-H]-	PG (18:3/18:3)	Lipids	1.21 E+05	1.16E +05	1.23E +05	1.38E +05*
22.94 1	317.24 02	[M-H]-	FA 21:4	Lipids	4.18 E+02	3.22E +02	4.27E +02	3.30E +02*
23.04 1	738.49 48	[M-H]-	PE (18:2/18:2)	Lipids	5.00 E+05	4.45E +05*	5.58E +05*	5.92E +05*
23.14 5	281.24 61	[M+H] +	FA 18:2 (Linoleic acid) ^a	Lipids	1.86 E+06	2.63E +06*	2.86E +06*	3.16E +06*
23.19 8	831.48 82	[M-H]-	PI (16:0/18:3)	Lipids	9.52 E+04	1.13E +05*	1.23E +05*	1.21E +05*
23.24 1	857.49 95	[M-H]-	PI (18:2/18:2)	Lipids	2.42 E+05	2.94E +05*	4.35E +05*	4.42E +05*
23.39 9	729.45 94	[M-H]-	PG (15:0/18:3)	Lipids	3.82 E+05	4.26E +05	4.32E +05*	4.41E +05*
23.46 9	307.25 73	[M-H]-	FA 20:2	Lipids	3.21 E+03	3.38E +03	4.17E +03*	5.94E +03

23.51 6	705.43 63	[M-H]-	PMeOH (18:3/18:3)	Lipids	3.39 E+05	4.71E +05*	2.60E +05*	2.91E +05
23.55 4	269.25 09	[M-H]-	FA 17:0	Lipids	2.51 E+04	2.57E +04	2.78E +04*	2.52E +04
23.77 5	833.53 86	[M-H]-	PI (16:0/18:2)	Lipids	6.34 E+06	7.24E +06	1.06E +07*	1.06E +07*
23.79 5	655.42 62	[M-H]-	PMeOH (14:0/18:3)	Lipids	2.70 E+04	3.75E +04*	1.98E +04*	2.14E +04*
23.82 7	743.46 89	[M-H]-	PG (16:0/18:3)	Lipids	4.21 E+07	4.57E +07*	4.65E +07*	4.88E +07*
23.85 9	769.48 81	[M-H]-	PG (18:2/18:2)	Lipids	1.09 E+06	1.18E +06*	1.29E +06*	1.23E +06*
23.92 2	859.52 03	[M-H]-	PI (18:1/18:2)	Lipids	9.83 E+04	1.15E +05*	2.05E +05*	2.04E +05*
23.98 5	731.51 20	[M-H]-	PG (15:0/18:2)	Lipids	7.98 E+05	8.30E +05	8.84E +05*	9.62E +05*
23.98 5	753.49 36	[M-H]-	PG (O-18:3/18:2)	Lipids	2.89 E+04	3.44E +04*	3.96E +04*	4.39E +04*
24.13 3	672.50 64	[M-H]-	PE (O-14:0/18:2)	Lipids	1.81 E+04	1.77E +04	1.25E +04*	1.53E +04*
24.15 5	707.45 47	[M-H]-	PMeOH (18:2/18:3)	Lipids	1.82 E+06	2.44E +06*	1.38E +06*	1.42E +06*
24.31 3	719.46 50	[M-H]-	PG (16:0/16:1)	Lipids	3.14 E+07	3.35E +07	3.68E +07	3.92E +07*
24.34 5	757.50 89	[M-H]-	PG (17:0/18:3)	Lipids	2.80 E+05	3.06E +05	4.29E +05*	4.82E +05*
24.34 5	669.44 41	[M-H]-	PMeOH (15:0/18:3)	Lipids	1.20 E+05	1.70E +05*	1.15E +05	1.24E +05
24.52 0	657.44 00	[M-H]-	PMeOH (14:0/18:2)	Lipids	2.04 E+04	2.99E +04*	2.20E +04	2.17E +04
24.52 4	847.52 61	[M-H]-	PI (17:0/18:2)	Lipids	7.80 E+04	7.31E +04	1.50E +05*	1.84E +05*
24.59 8	745.49 14	[M-H]-	PG (16:0/18:2)	Lipids	2.23 E+07	2.75E +07*	2.93E +07*	3.10E +07*
24.72 5	771.50 64	[M-H]-	PG (18:1/18:2)	Lipids	1.60 E+04	1.97E +04	3.06E +04*	3.28E +04*
25.00 5	309.27 40	[M-H]-	FA 20:1	Lipids	5.60 E+04	6.04E +04*	6.76E +04*	7.64E +04

^a Confirmed by the standard database; * metabolites with significant differences compared to the control.