Figure S1. Representative UHPLC-QTOF-MS chromatogram for the negative ionization mode of *O. ficus* methanolic extract incubated with the selected microbial strains at a concentration of 5 mg/ml after 0.5 h (black) and 24 h (red), both chromatograms are characterized by three regions; (50-500 s for phenolic and organic acids, (400-900 s) for flavonoids, and (750-1450 s) for fatty acids
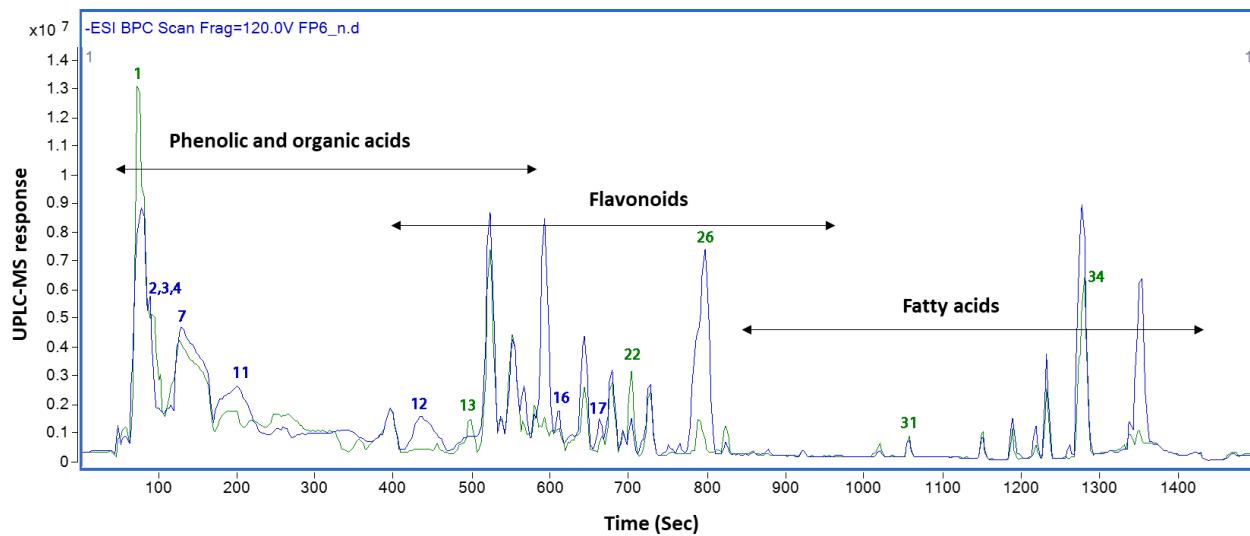

Figure S2. Representative UHPLC-QTOF-MS chromatogram for the negative ionization mode of untreated *O. ficus* methanolic extract (green) and treated *ex-vivo* (blue) with bacterial culture isolated from actual fecal matter at a concentration of 10 mg/ml, both chromatograms are characterized by three regions; (50-530 s for phenolic and organic acids, (400-1000 s) for flavonoids, and (710-1370 s) for fatty acids
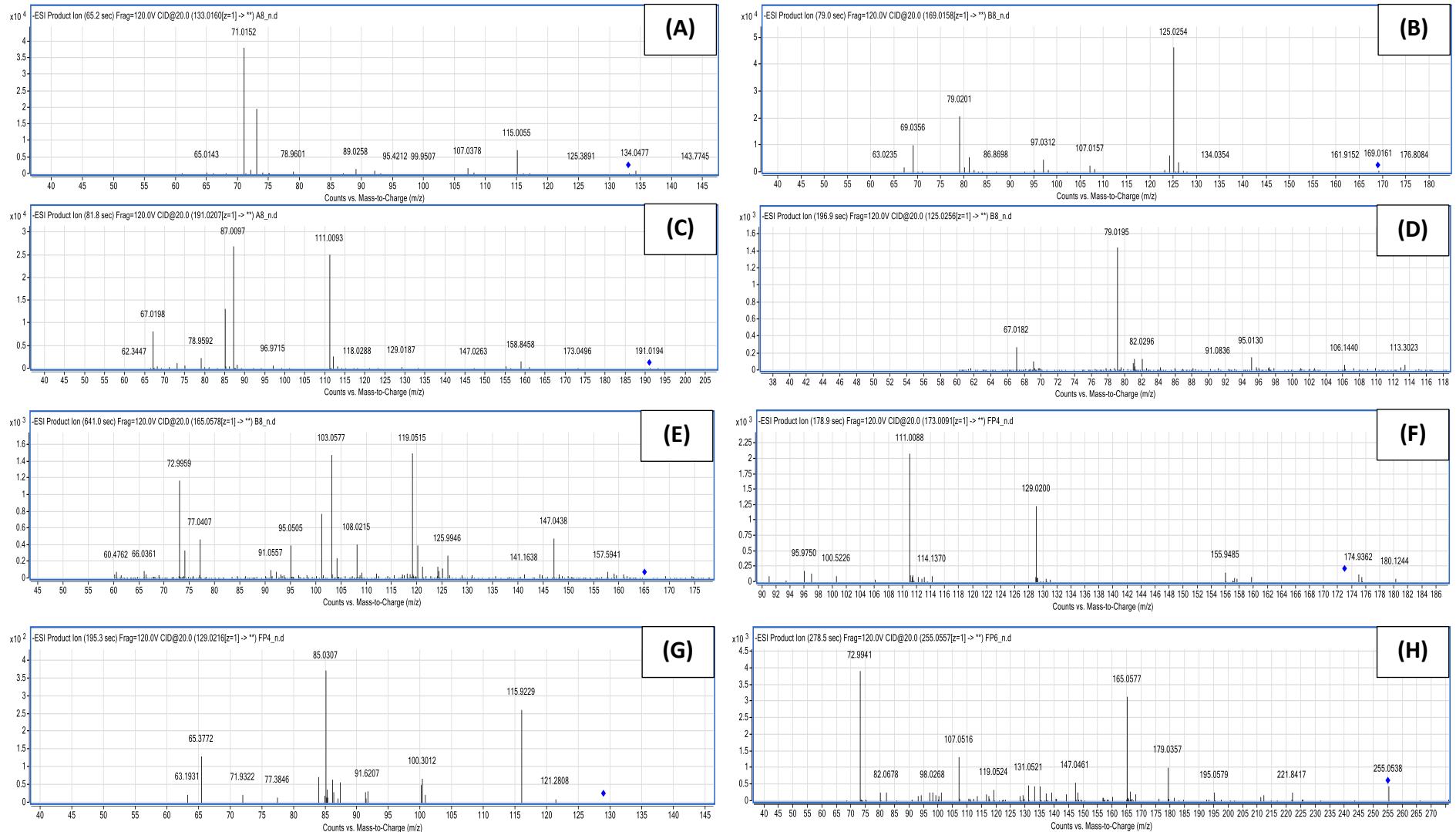
Figure S3. Tandem mass spectral data of some of the major metabolites studied in in vitro and ex vivo assays namely; A) Malic acid, B) Gallic acid, C) (iso)Citric acid, D) Phloroglucinol, E) 3-(4-Hydroxyphenyl) propanoic acid, F) Aconitic acid, G) Mesaconic acid, H) Piscidic acid.
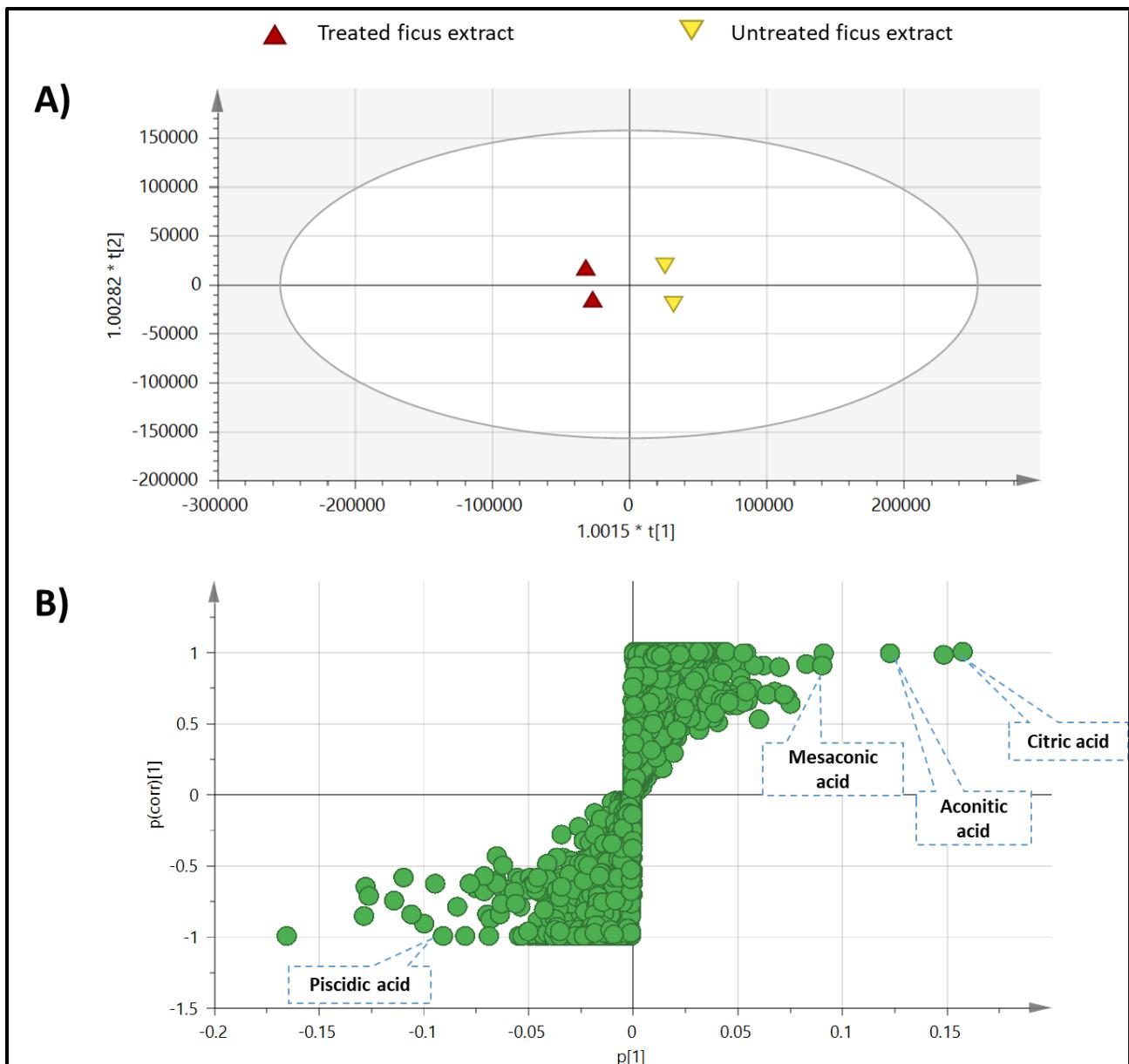
Figure S4. (A) OPLS model of *O. ficus* treated *ex-vivo* with gut microbiota culture isolated form fecal matter based on treatment; untreated samples (yellow) modeled against treated (red) B) S-plot of OPLS model, metabolites with positive p[1] values indicates higher abundance in untreated sample mainly; (iso)citric, aconitic and mesaconic acids, while negative p[1] indicates higher abundance within treated sample mainly; piscidic acid.

Table S1. Metabolites identified in *O. ficus* samples treated with gut microbiota at two time intervals; 0.5 and 24 h along with their relative abundance. Results are expressed as relative percentile (average ± std deviation, n=3) of the total peak areas of identified metabolites.

Peak No.	[M-H]⁻	Name	Abundance % at 0.5 h	Abundance % at 24 h
1	133.0154	Malic acid*	9.38±0.57	2.09±1.06
2	169.0161	Gallic acid*	9.2±2.85	14.2±0.36
3	189.0057	(iso)Citrate*	50.79±2.11	40.12±1.96
4	207.0159	Hydroxycitric acid*	1.69±0.11	1.32±0.38
5	125.0256	Pyrogallol*	0	4.57±0.73
6	117.0204	Succinic acid*	7.22±1.32	12.43±3.81
7	125.0257	Phloroglucinol*	0	2.01±0.81
8	205.0368	Homocitric acid*	2.52±0.18	0
9	153.0214	Protocatechuic acid	0.11±0.04	0
10	199.0265	Fumarylacetoacetic acid (Maleylacetoacetic acid)*	0.8±0.06	3.15±0.33
11	117.0566	Hydroxyvaleric acid*	1.11±0.77	1.95±0.17
12	541.2307	Isorhamnetin glycoside*	2.06±0.4	1.69±0.17
13	219.0532	Dimethyl citrate	9.45±0.42	8.45±0.5
14	183.032	Methyl gallate	1.54±0.03	1.01±0.04
15	165.0585	3-(4-Hydroxyphenyl) propanoic acid*	0	3.57±0.704
16	563.1102	Kaempferol*	0	0.13±0.01
17	301.0387	Quercetin glycoside	0.45±0.07	0.22±0.03
18	349.0618	Ethyl gallate derivative	0.12±0.01	0
19	285.043	Quercetin	0.26±0.01	0.48±0.07
20	271.0627	Naringenin	0.11±0.01	0
21	287.2249	Dihydroxyhexadecanoic acid*	0.05±0.01	0.11±0.01
22	443.1753	Trihydroxyoctadecenoic acid derivative	0.12±0.01	0.07±0.01
23	329.2358	Trihydroxyoctadecenoic acid*	0	0.15±0.01
24	663.2948	Dihydroxyhexadecanoic acid derivative*	0.69±0.05	0
25	547.2805	Dihydroxyhexadecanoic acid derivative	0.29±0.02	0.11±0.01
26	269.0472	Apigenin	0.41±0.04	0.88±0.05
27	299.0597	Diosmetin*	0.08±0.01	0
28	283.0643	Acacetin*	0.12±0.01	0
29	277.1822	Panaxytriol	0	0.49±0.07
30	483.3161	Palmitic acid derivative	0.05±0.01	0
31	239.0701	Hydroxyflavanone*	0.05±0.01	0
32	295.2301	Hydroxylinoleic acid	0.15±0.03	0
33	243.1984	Hydroxytetradecanoic acid	0.077±0.019	0
34	271.2278	Hydroxyhexadecanoic acid	0.14±0.01	0.39±0.06
35	471.3509	Hydroxybetulinic acid	0.06±0.01	0

Peak No.	[M-H]$^-$	Name	Abundance % at 0.5 h	Abundance % at 24 h
36	253.2196	Palmitoleic acid (Hexadecenoic acid)	0.02±0.01	0
37	279.2351	Linoleic acid*	0.25±0.02	0
38	255.2355	Palmitic acid (Hexadecanoic acid)	0.09±0.02	0.22±0.04
39	281.2521	Oleic acid*	0.34±0.01	0

* Denotes metabolites that showed significant difference when analyzed using paired t test (p value < 0.05)

Table S2. Metabolites identified in *O. ficus* samples; untreated and treated with ex vivo culture of the human gut microbiome isolated from fecal matter along with their relative abundance

Peak No.	[M-H]$^-$	Rt $_{(sec)}$	Molecular Formula	Error (ppm)	MS/MS	Name	Class	Untreated *O. ficus* sample	*O. ficus* treated with culture of the human gut microbiome
1	195.0504	66	$C_6H_{12}O_7$	3.19	177.01, 133.03	Gluconic acid	Organic acids	++	+
2	353.0862	83	$C_{16}H_{18}O_9$	4.53	191.01	Caffeoylquinic acid	Phenolic acid	+	-
3	73.0311	97	$C_3H_6O_2$	-8.2	-	Propionic acid	SCFA	-	+
4	133.0137	98	$C_4H_6O_5$	4.08	115, 71.01	Malic acid	Organic acid	+	-
5	205.0356	101	$C_7H_{10}O_7$	-1.09	191.05, 127, 111.01	Homocitric acid	Organic acid	++	+
6	191.0193	110	$C_6H_8O_7$	3.26	171.03, 127, 111, 99, 83.01	(iso)citric acid	Organic acid	+	-
7	117.0211	126	$C_4H_6O_4$	-14.98	73.03	Succinic acid	Organic acid	-	+
8	173.0091	180	$C_6H_6O_6$	-16.89	129.02, 111.01, 85.03	Aconitic acid	Organic acid	++	+
9	129.0216	188	$C_5H_6O_4$	2.56	85.05	Mesaconic acid	Organic acid	+	-
10	147.0454	190	$C_9H_8O_2$	-1.67	129.01, 103.03, 85.01	Cinnamic acid	Phenolic acid	++	+

Peak No.	[M-H]⁻	Rt (sec)	Molecular Formula	Error (ppm)	MS/MS	Name	Class	Untreated *O. ficus* sample	*O. ficus* treated with culture of the human gut microbiome
11	255.0557	268	$C_{11}H_{12}O_7$	-0.29	165.05, 119.05, 107.05	Piscidic acid	Phenolic acid	+	++
12	117.0557	412	$C_5H_{10}O_3$	0.15	99.02	Hydroxypentanoic acid (hydroxyvaleric acid)	SCFA	+	++
13	431.1043	508	$C_{21}H_{20}O_{10}$	-13.72	285.11	Kaempferol rhamnoside	Flavonoids	+	-
14	331.0681	527	$C_{13}H_{16}O_{10}$	-3.1	169.01	Galloylglucose	Phenolics	+	-
15	473.2102	602	$C_{22}H_{34}O_{11}$	-13.21	301.11, 179.07, 151	Quercetin glycoside	Flavonoids	++	+
16	285.0376	616	$C_{15}H_{10}O_6$	10	268.03, 243.03, 195.04, 169.06	Kaempferol	Flavonoids	-	+
17	165.0592	643	$C_9H_{10}O_3$	-14.97	147.03, 119.05, 91.01	3-(4-Hydroxyphenyl) propanoic acid	Phenolics	-	+
18	423.0918	652	$C_{19}H_{20}O_{11}$	3.5	331.09, 169.01	Galloylarbutin	Phenolics	+	-
19	609.1450	673	$C_{27}H_{30}O_{16}$	10.01	447.01, 315.15	Isorhamnetin-O-pentosyl-hexoside	Flavonoids	+	-
20	445.0502	674	$C_{20}H_{14}O_{12}$	14.14	301.14, 179.07, 151	Quercetin glycoside	Flavonoids	++	+
21	437.1138	695	$C_{20}H_{22}O_{11}$	11.1	331.01, 169.01	Galloylglucose derivative	Phenolics	+	-
22	443.1824	709	$C_{17}H_{32}O_{13}$	-12.12	329.23, 133.01, 71.01	Trihydroxyoctadecenoic acid derivative	Fatty acids	++	+

Peak No.	[M-H]⁻	Rt (sec)	Molecular Formula	Error (ppm)	MS/MS	Name	Class	Untreated O. ficus sample	O. ficus treated with culture of the human gut microbiome
23	541.2636	725	$C_{26}H_{38}O_{12}$	3.39	315.11	Isorhamnetin glycoside	Flavonoids	++	+
24	785.2930	746	$C_{29}H_{54}O_{24}$	0.29	315.29	Isorhamnetin glycoside	Flavonoids	+	-
25	477.0217	787	$C_{20}H_{14}O_{14}$	12.09	331.01, 169.01	Galloylglucose derivative	Phenolics	+	-
26	329.2304	823	$C_{18}H_{34}O_5$	8.43	133.01, 71.01	Trihydroxyoctadecenoic acid	Fatty acids	+	++
27	533.2029	824	$C_{27}H_{34}O_{11}$	-0.83	329.23	Trihydroxyoctadecenoic acid derivative	Fatty acids	++	+
28	301.0327	863	$C_{15}H_{10}O_7$	8.86	179.07, 151	Quercetin	Flavonoids	-	+
29	235.1736	945	$C_{15}H_{24}O_2$	-13.95	217.17, 191.01	Farnesoic acid	Fatty acids	+	-
30	271.0641	1015	$C_{15}H_{12}O_5$	-10.67	253.15, 209.36, 177.37, 151.01, 119.04	Naringenin	Flavonoids	-	+
31	295.2328	1057	$C_{18}H_{32}O_3$	-16.65	277.21, 251, 183.13	Hydroxylinoleic acid	Fatty acids	++	+
32	281.2513	1156	$C_{18}H_{34}O_2$	-9.55	237.03, 171.1	Oleic acid	Fatty acids	+	-
33	279.2364	1223	$C_{18}H_{32}O_2$	-12.3	237.09, 187.01	Linoleic acid	Fatty acids	++	+
34	323.226	1272	$C_{19}H_{32}O_4$	-9.83	255.23	Palmitic acid derivative	Fatty acids	+	-

* ++, +, -; reflects the metabolite relative abundance as depicted from the peak abundance data extracted from MS-DIAL, (++) increased abundance, (+) present, (-) absent

Table S3. Metabolites identified in *O. ficus* untreated and treated ex-vivo with actual fecal matter samples along with their relative abundance. Results are expressed as relative percentile (average ± std deviation, n=3) of the total peak areas of identified metabolites.

Peak No.	[M-H]⁻	Name	Abundance % at untreated sample	Abundance % at treated sample
1	195.0504	Gluconic acid*	2.72±0.12	1.26±0.05
2	353.0862	Caffeoylquinic acid	0.65±0.01	0.15±0.01
3	73.0311	Propionic acid*	0	1.43±0.02
4	133.0137	Malic acid*	7.75±0.01	1.81±0.01
5	205.0356	Homocitric acid*	2.95±0.51	0.71±0.01
6	191.0193	Citric acid*	32.52±0.9	0.56±0.03
7	117.0211	Succinic acid*	0.69±0.3	37.96±0.93
8	173.0121	Aconitic acid*	19.73±0.08	0.31±0.0
9	129.0190	Mesaconic acid*	6.92±0.41	0.11±0.0
10	147.0454	Cinnamic acid*	1.37±0.01	0.41±0.0
11	255.0511	Piscidic acid*	2.34±0.03	29.76±0.87
12	117.0557	Hydroxypentanoic acid*	0.24±0.0	1.99±0.01
13	431.1043	Kaempferol rhamnoside*	1.11±0.06	0.03±0.0
14	331.0681	Galloylglucose*	0.31±0.01	0
15	473.2102	Quercetin glycoside*	1.82±0.03	0.07±0.0
16	285.0242	Kaempferol*	0	2.69±0.07
17	165.0592	3-(4-Hydroxyphenyl) propanoic acid*	0	2.31±0.02
18	423.0918	Galloylarbutin	0.61±0.02	0.03±0.0
19	609.1450	Isorhamnetin-O-pentosyl-hexoside	0.21±0.01	0
21	437.1138	Galloylglucose derivative*	1.26±0.05	0.15±0.01
21	445.0502	Quercetin glycoside*	2.63±0.01	0.18±0.02
22	443.1824	Trihydroxyoctadecenoic acid derivative*	1.87±0.05	0
25	477.0217	Galloylglucose derivative*	1.05±0.05	0.22±0.01
26	329.2304	Trihydroxyoctadecenoic acid*	0.58±0.05	4.22±0.01
27	541.2636	Isorhamnetin glycoside*	2.77±0.12	0.26±0.01
27	533.2029	Trihydroxyoctadecenoic acid derivative	0.38±0.01	0.15±0.0
28	785.2930	Isorhamnetin glycoside*	2.31±0.09	0.45±0.02
29	301.0327	Quercetin*	0.13±0.01	3.16±0.02
29	235.1736	Farnesoic acid	0.24±0.03	0.03±0.0
31	295.2328	Hydroxylinoleic acid*	2.01±0.02	0.26±0.01
32	271.0641	Naringenin*	0.11±0.02	3.62±0.02
32	281.2513	Oleic acid*	1.11±0.07	0

Peak No.	[M-H]⁻	Name	Abundance % at untreated sample	Abundance % at treated sample
33	279.2364	Linoleic acid	0.83±0.03	0.15±0.0
34	323.226	Palmitic acid derivative*	0.92±0.05	0

* Denotes metabolites that showed significant difference when analyzed using paired t test (p value < 0.05)