Supplementary Material

Comprehensive Metabolites Fingerprinting of Australian Black and Green Olives and Their Antioxidant and Pharmacokinetics Properties

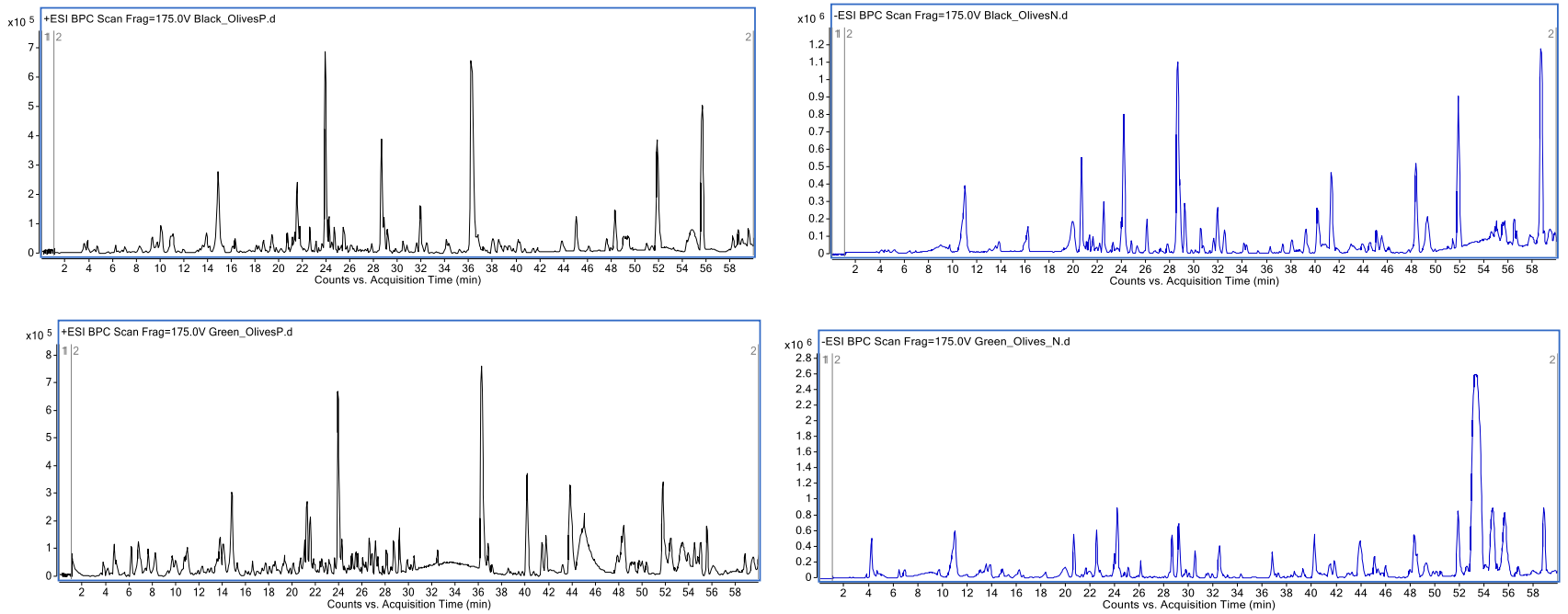
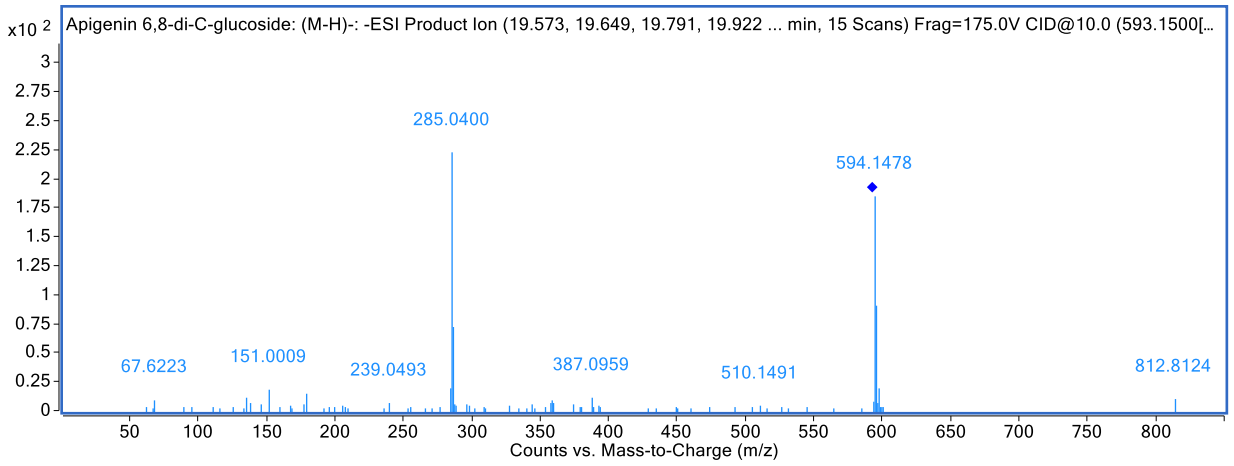
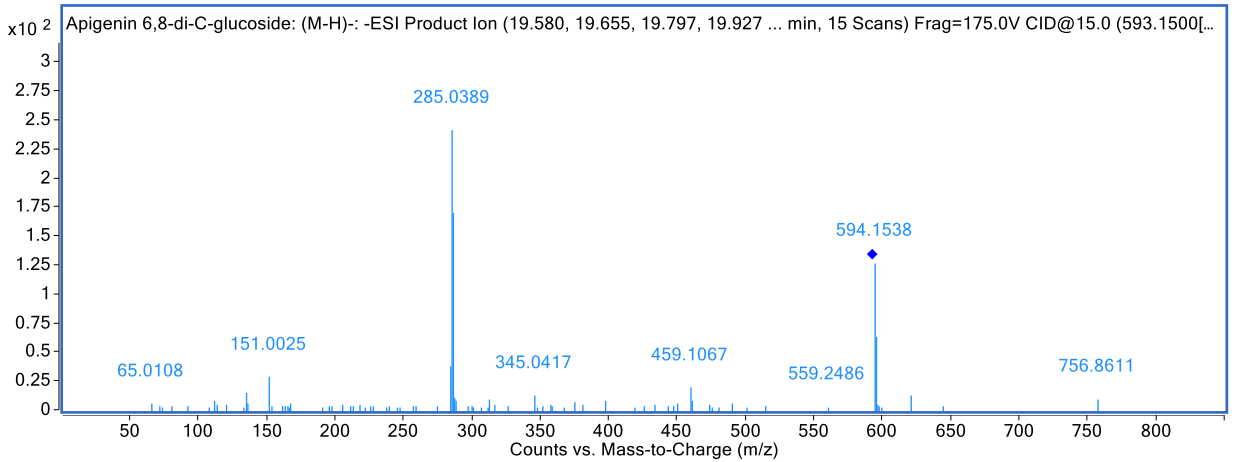
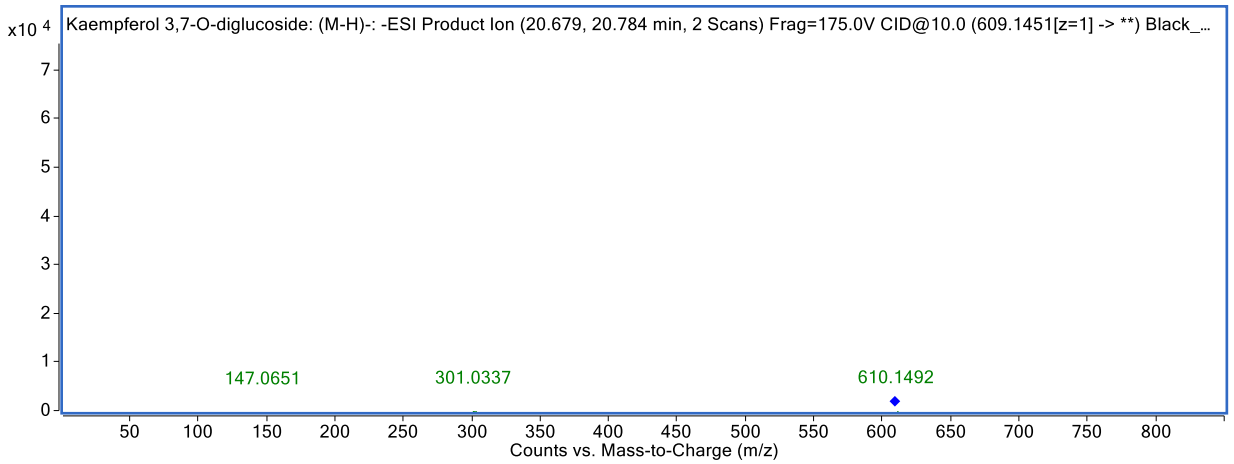
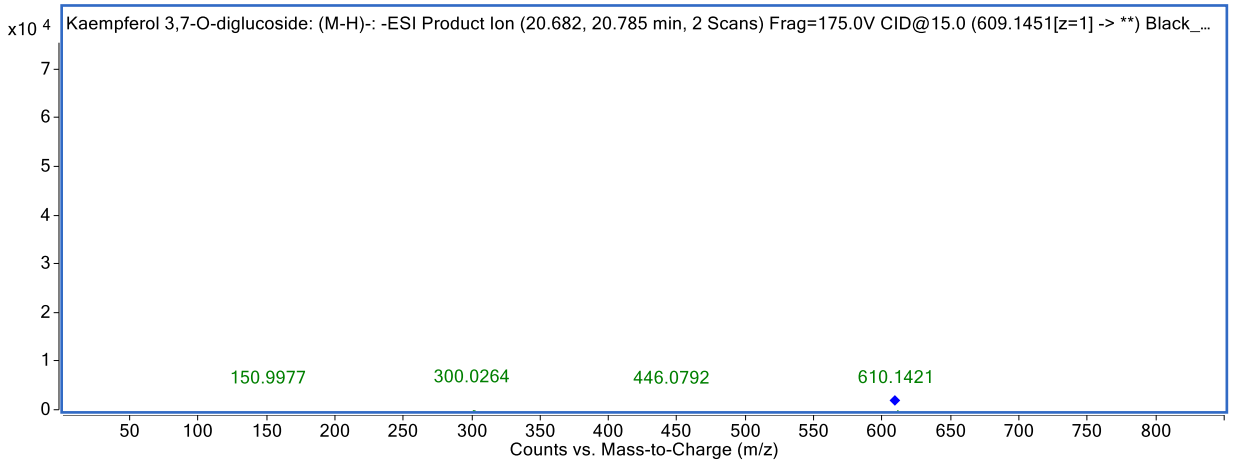


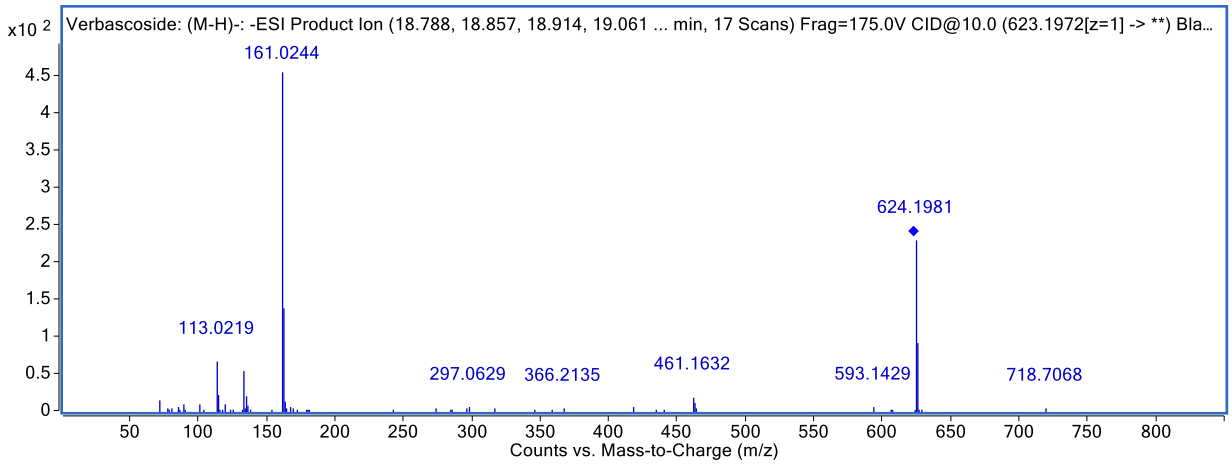
Figure S1. Base peak chromatograms (BPC) of black and green olives in positive (black) and negative (blue) modes

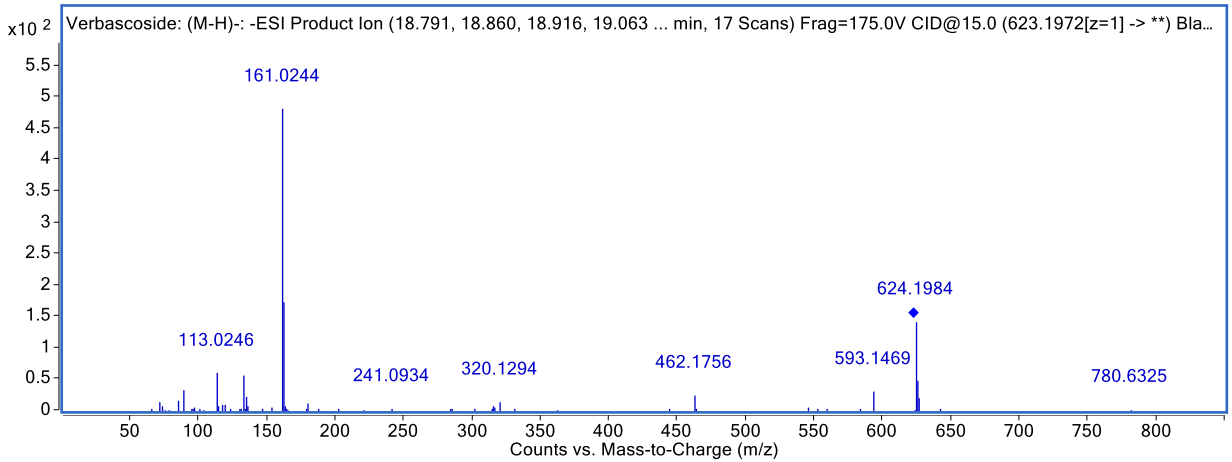

Apigenin 6,8-di-C-glucoside: (M-H)-: -ESI Product Ion (19.573, 19.649, 19.791, 19.922 ... min, 15 Scans) Frag=175.0V CID@10.0 (593.1500[...
x10 2
285.0400
594.1478
67.6223
151.0009
239.0493
387.0959
510.1491
812.8124
Counts vs. Mass-to-Charge (m/z)

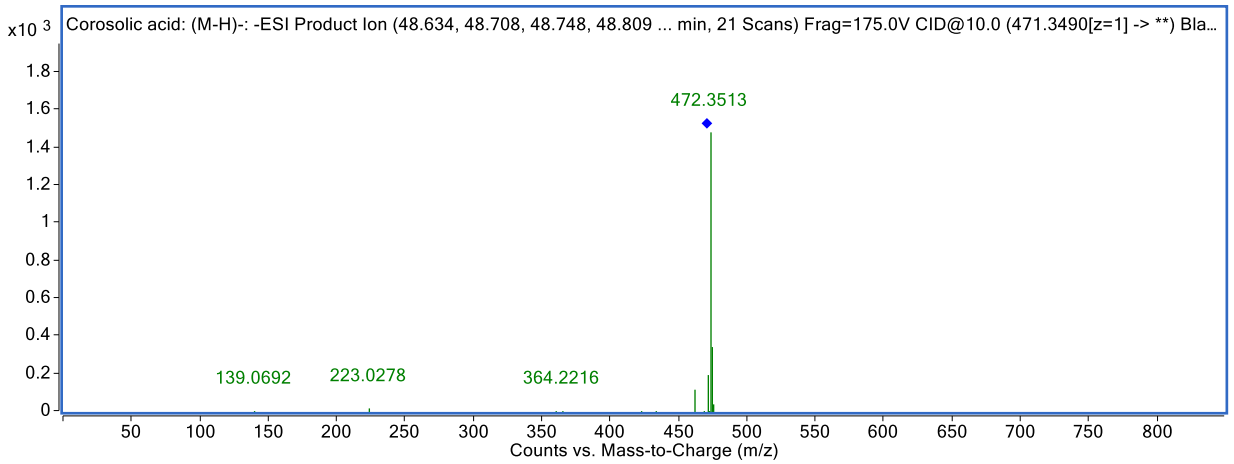

Apigenin 6,8-di-C-glucoside: (M-H)-: -ESI Product Ion (19.580, 19.655, 19.797, 19.927 ... min, 15 Scans) Frag=175.0V CID@15.0 (593.1500[...
x10 2
285.0389
594.1538
65.0108
151.0025
345.0417
459.1067
559.2486
756.8611
Counts vs. Mass-to-Charge (m/z)

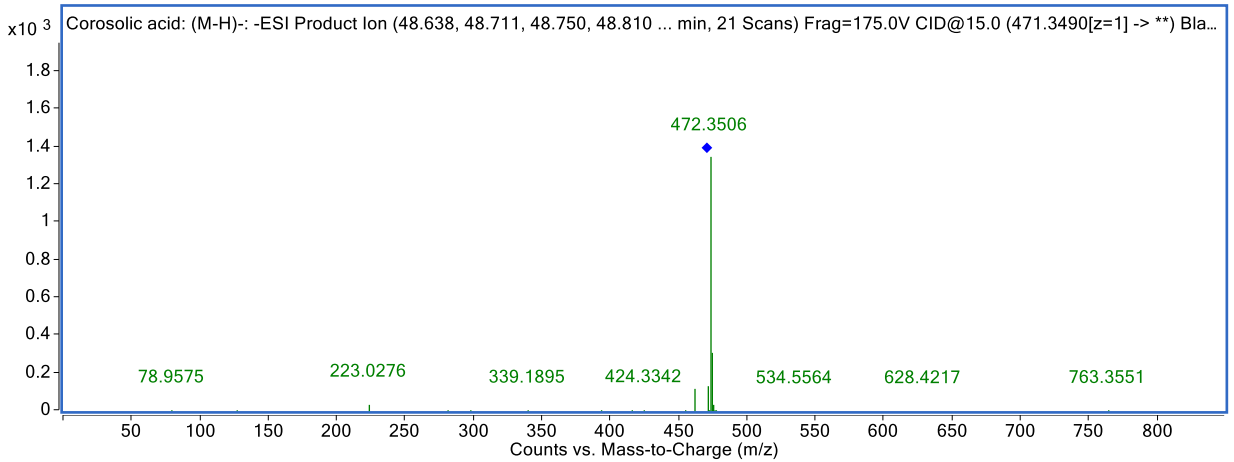

x10 4
Kaempferol 3,7-O-diglucoside: (M-H)-: -ESI Product Ion (20.679, 20.784 min, 2 Scans) Frag=175.0V CID@10.0 (609.1451[z=1] -> **) Black_...
147.0651
301.0337
610.1492
Counts vs. Mass-to-Charge (m/z)

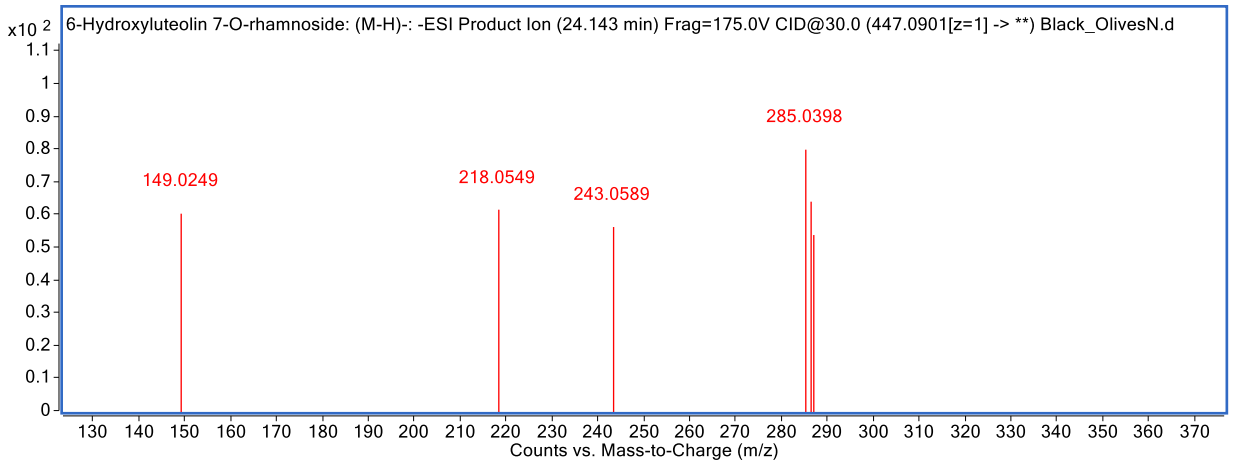

x10 4
Kaempferol 3,7-O-diglucoside: (M-H)-: -ESI Product Ion (20.682, 20.785 min, 2 Scans) Frag=175.0V CID@15.0 (609.1451[z=1] -> **) Black_...
150.9977
300.0264
446.0792
610.1421
Counts vs. Mass-to-Charge (m/z)

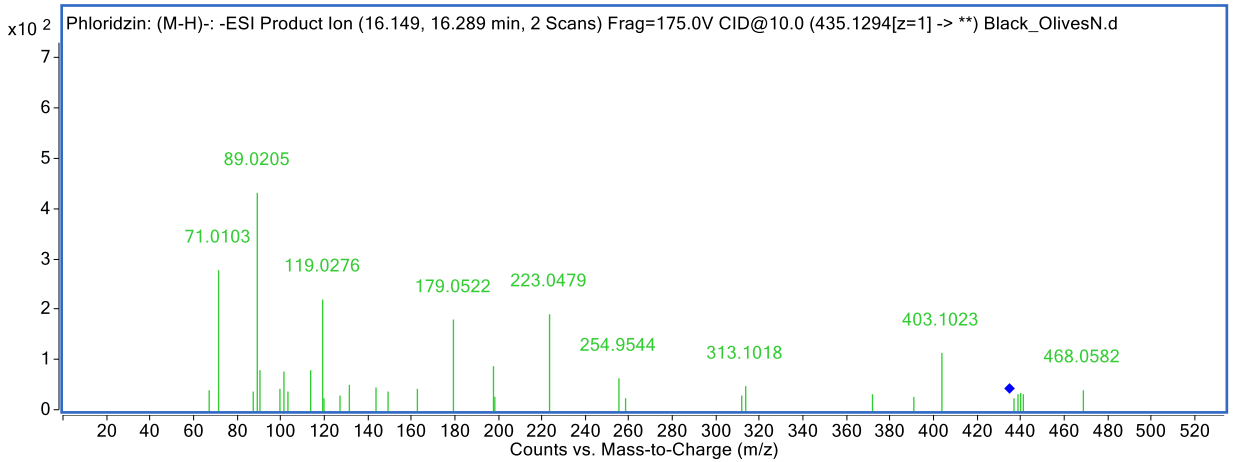

Verbascoside: (M-H)-: -ESI Product Ion (18.788, 18.857, 18.914, 19.061 ... min, 17 Scans) Frag=175.0V CID@10.0 (623.1972[z=1] -> **) Bla...
x10 2
161.0244
624.1981
113.0219
297.0629
366.2135
461.1632
593.1429
718.7068
Counts vs. Mass-to-Charge (m/z)

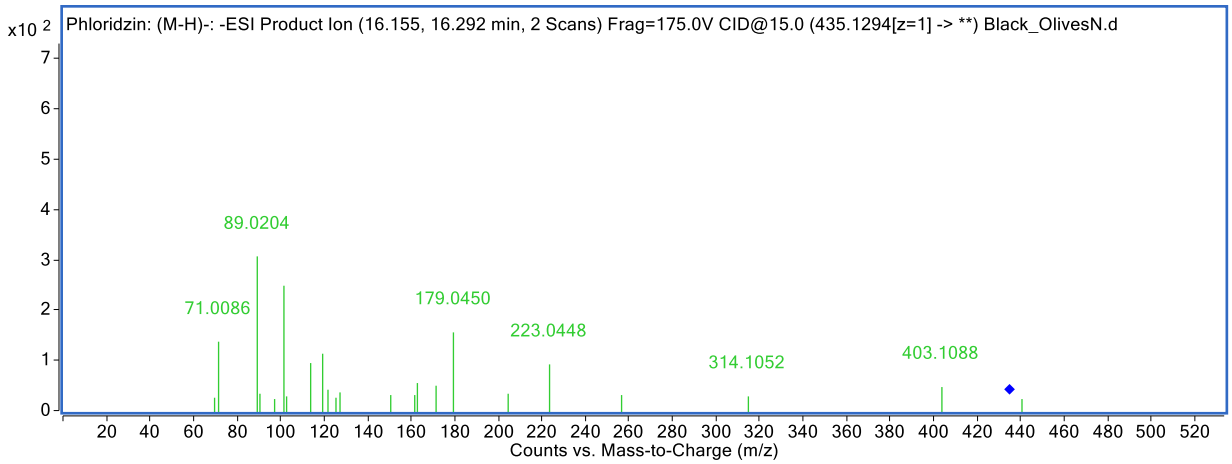

Verbascoside: (M-H)-: -ESI Product Ion (18.791, 18.860, 18.916, 19.063 ... min, 17 Scans) Frag=175.0V CID@15.0 (623.1972[z=1] -> **) Bla...
x10 2
161.0244
624.1984
113.0246
241.0934
320.1294
462.1756
593.1469
780.6325
Counts vs. Mass-to-Charge (m/z)

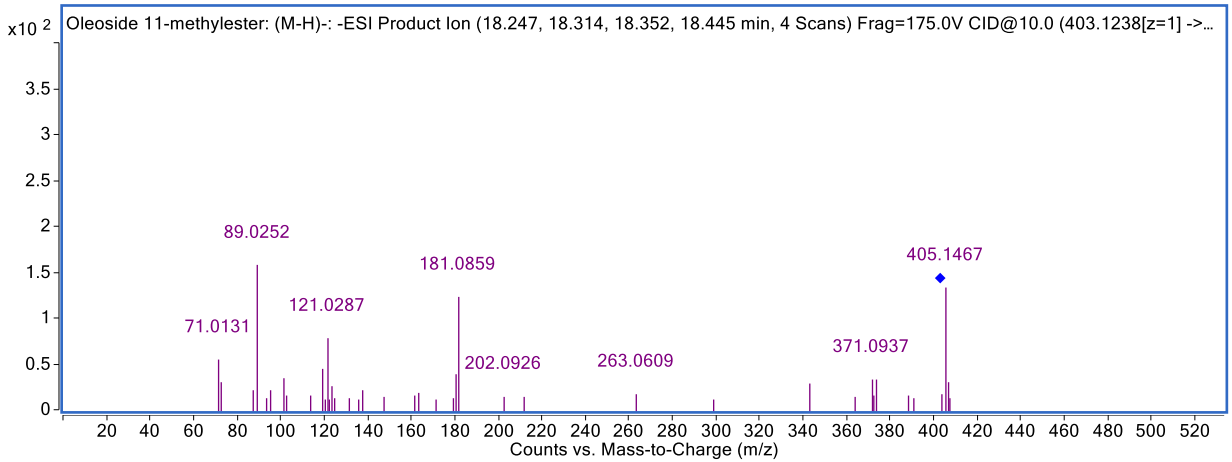

Corosolic acid: (M-H)-: -ESI Product Ion (48.634, 48.708, 48.748, 48.809 ... min, 21 Scans) Frag=175.0V CID@10.0 (471.3490[z=1] -> **) Bla...
x10 3
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
472.3513
139.0692
223.0278
364.2216
50 100 150 200 250 300 350 400 450 500 550 600 650 700 750 800
Counts vs. Mass-to-Charge (m/z)

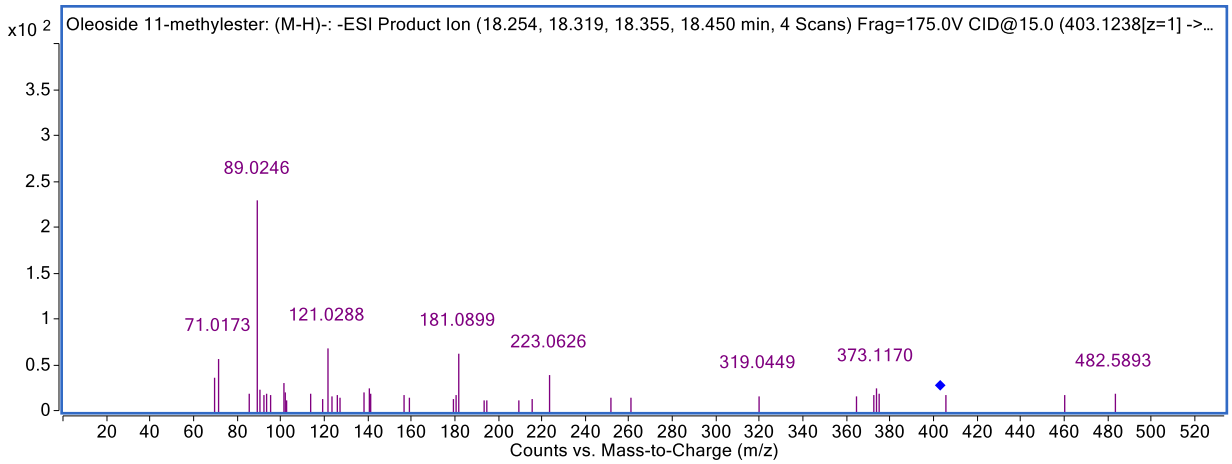

Corosolic acid: (M-H)-: -ESI Product Ion (48.638, 48.711, 48.750, 48.810 ... min, 21 Scans) Frag=175.0V CID@15.0 (471.3490[z=1] -> **) Bla...
x10 3
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
472.3506
78.9575
223.0276
339.1895
424.3342
534.5564
628.4217
763.3551
50 100 150 200 250 300 350 400 450 500 550 600 650 700 750 800
Counts vs. Mass-to-Charge (m/z)

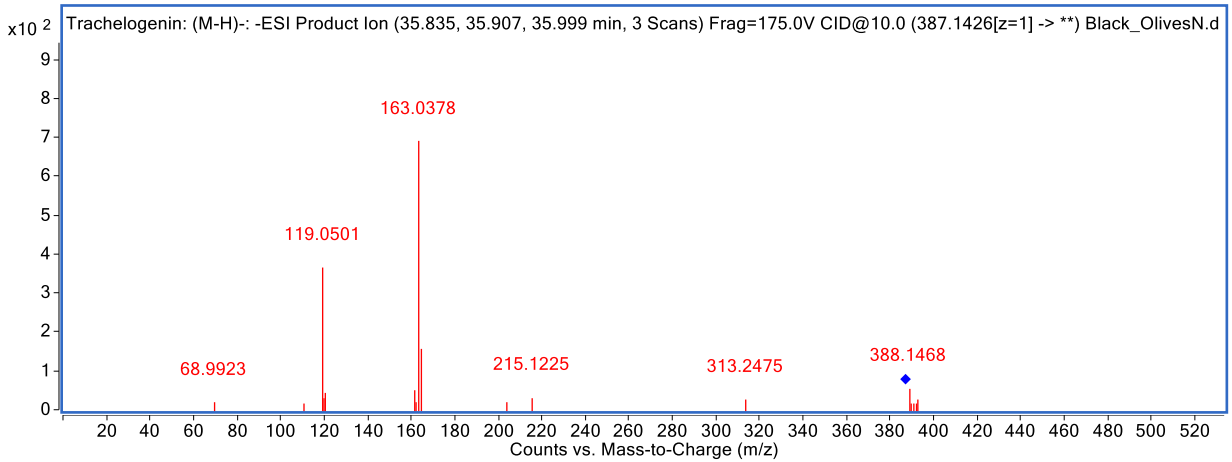

6-Hydroxyluteolin 7-O-rhamnoside: (M-H)-: -ESI Product Ion (24.143 min) Frag=175.0V CID@30.0 (447.0901[z=1] -> **) Black_OlivesN.d
x10 2
149.0249
218.0549
243.0589
285.0398
Counts vs. Mass-to-Charge (m/z)

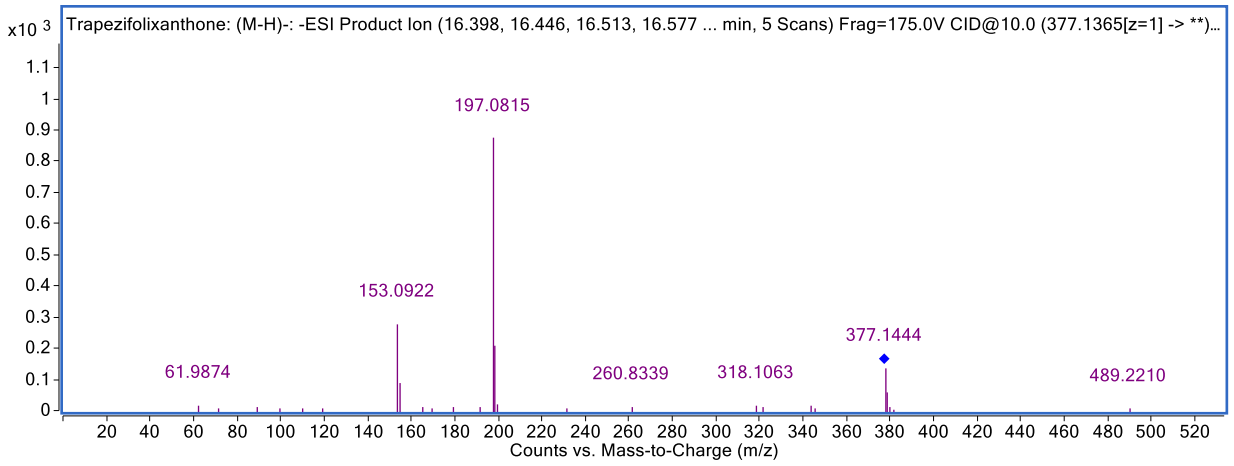

Phloridzin: (M-H)-: -ESI Product Ion (16.149, 16.289 min, 2 Scans) Frag=175.0V CID@10.0 (435.1294[z=1] -> **) Black_OlivesN.d
x10 2
89.0205
71.0103
119.0276
179.0522
223.0479
254.9544
313.1018
403.1023
468.0582
Counts vs. Mass-to-Charge (m/z)

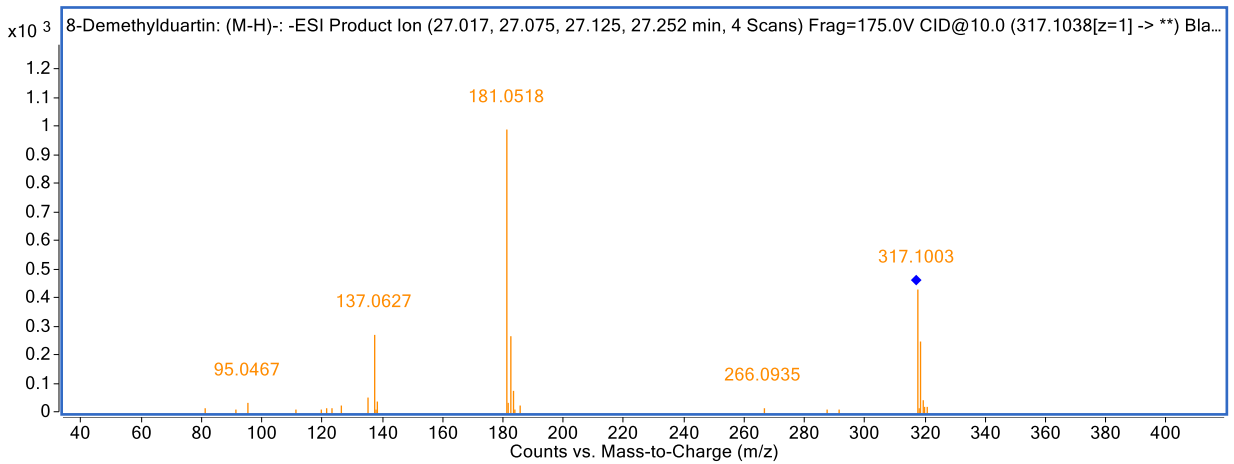

Phloridzin: (M-H)-: -ESI Product Ion (16.155, 16.292 min, 2 Scans) Frag=175.0V CID@15.0 (435.1294[z=1] -> **) Black_OlivesN.d
x10 2
89.0204
71.0086
179.0450
223.0448
314.1052
403.1088
Counts vs. Mass-to-Charge (m/z)

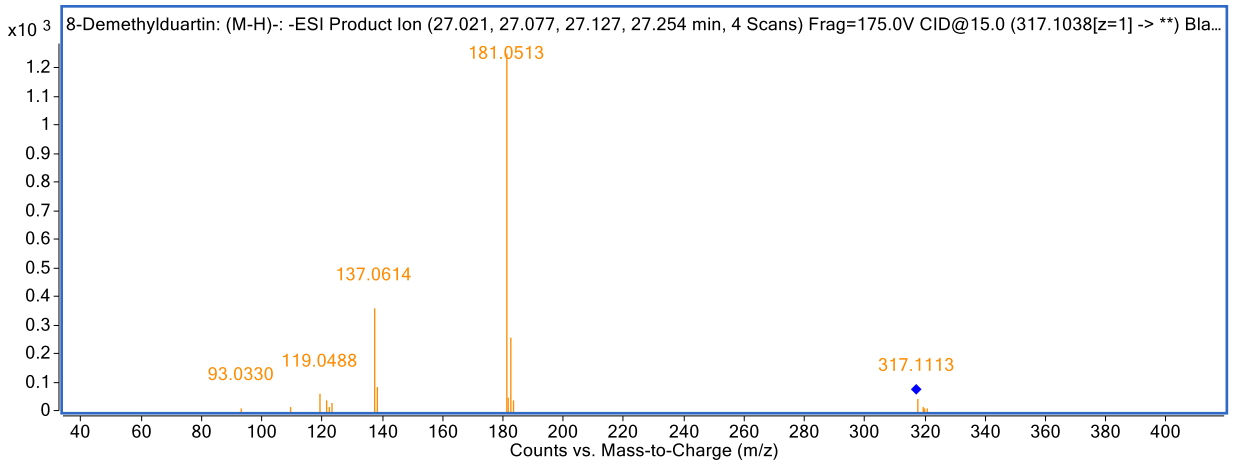

Oleoside 11-methylester: (M-H)-: -ESI Product Ion (18.247, 18.314, 18.352, 18.445 min, 4 Scans) Frag=175.0V CID@10.0 (403.1238[z=1] ->…
x10 2
89.0252
181.0859
405.1467
121.0287
71.0131
202.0926
263.0609
371.0937
Counts vs. Mass-to-Charge (m/z)

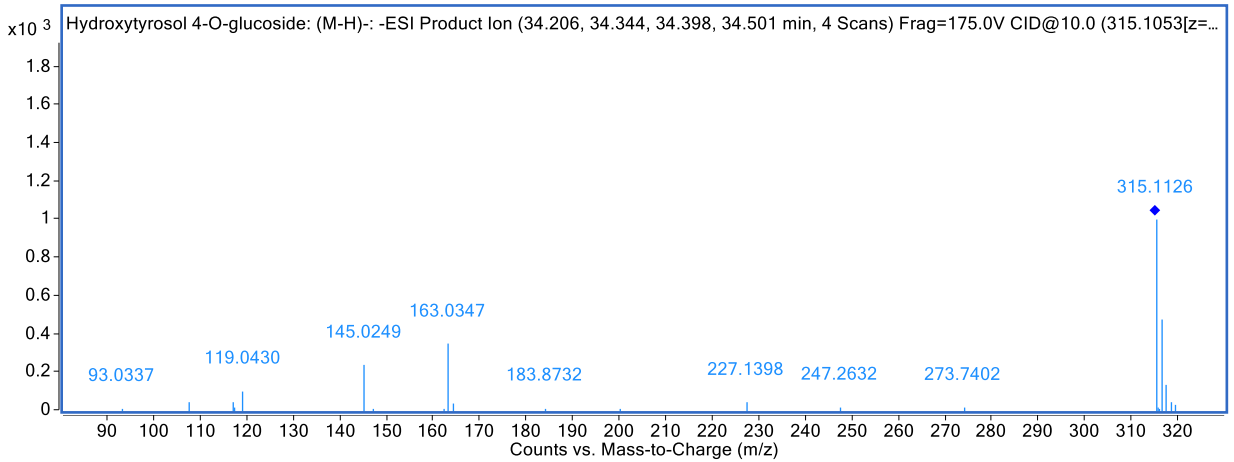

Oleoside 11-methylester: (M-H)-: -ESI Product Ion (18.254, 18.319, 18.355, 18.450 min, 4 Scans) Frag=175.0V CID@15.0 (403.1238[z=1] ->...
x10 2
89.0246
71.0173
121.0288
181.0899
223.0626
319.0449
373.1170
482.5893
Counts vs. Mass-to-Charge (m/z)

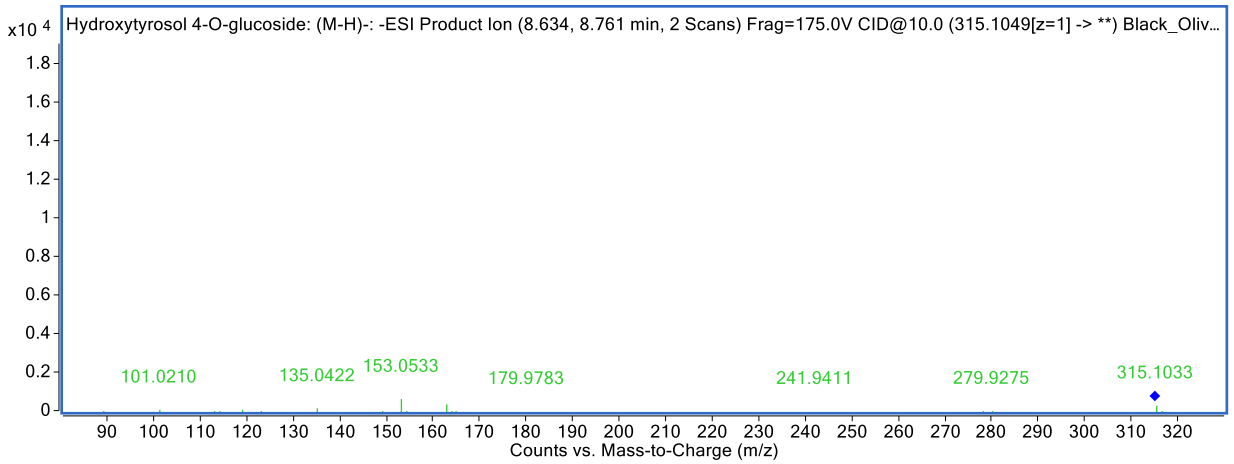

Trachelogenin: (M-H)-: -ESI Product Ion (35.835, 35.907, 35.999 min, 3 Scans) Frag=175.0V CID@10.0 (387.1426[z=1] -> **) Black_OlivesN.d
x10 2
163.0378
119.0501
68.9923
215.1225
313.2475
388.1468
Counts vs. Mass-to-Charge (m/z)

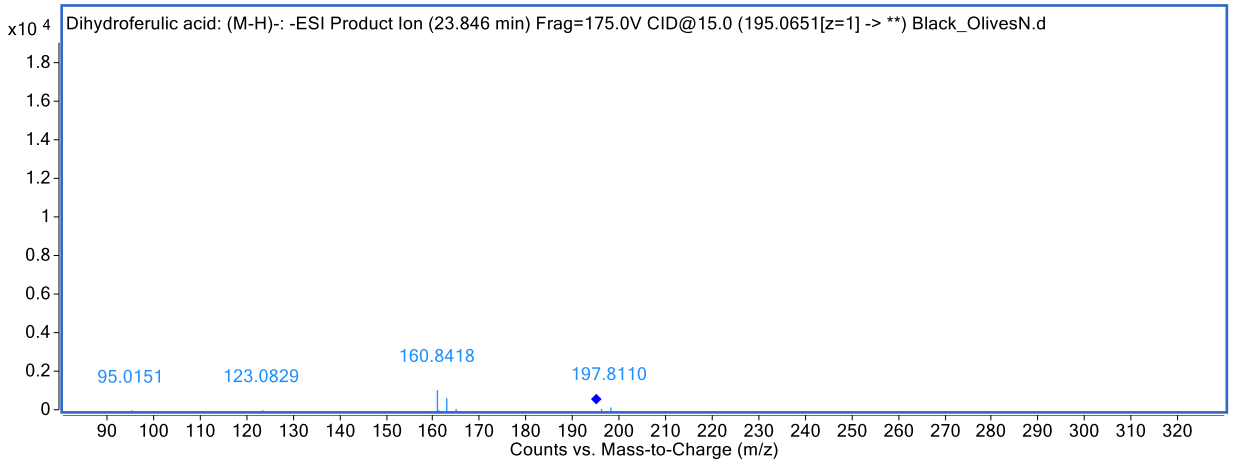

Trapezifolixanthone: (M-H)-: -ESI Product Ion (16.398, 16.446, 16.513, 16.577 ... min, 5 Scans) Frag=175.0V CID@10.0 (377.1365[z=1] -> **)...
x10 3
197.0815
153.0922
377.1444
61.9874
260.8339
318.1063
489.2210
Counts vs. Mass-to-Charge (m/z)


8-Demethylduartin: (M-H)-: -ESI Product Ion (27.017, 27.075, 27.125, 27.252 min, 4 Scans) Frag=175.0V CID@10.0 (317.1038[z=1] -> **) Bla...
x10 3
181.0518
317.1003
137.0627
95.0467
266.0935
Counts vs. Mass-to-Charge (m/z)

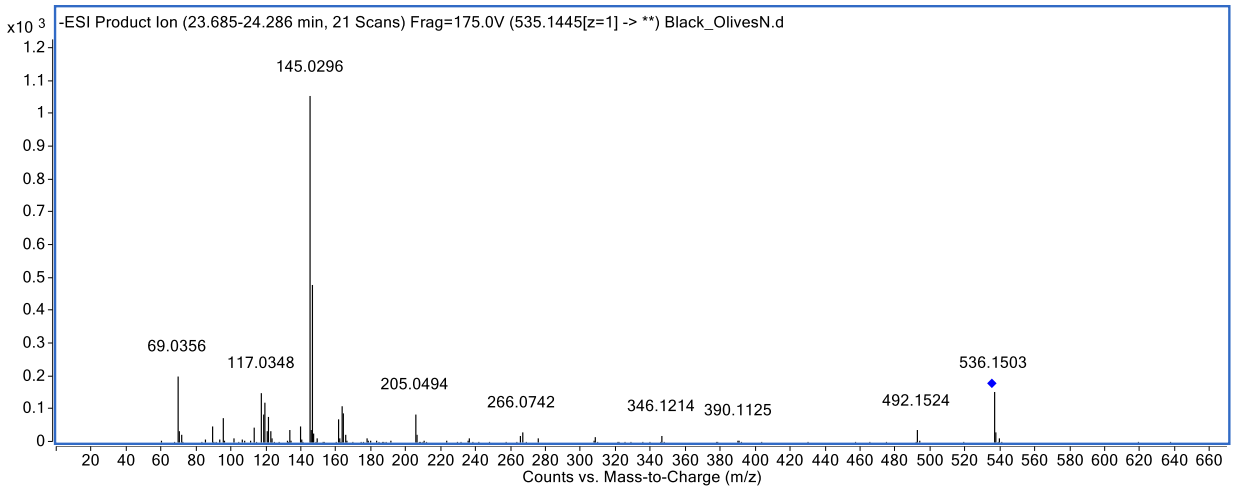

8-Demethylduartin: (M-H)-: -ESI Product Ion (27.021, 27.077, 27.127, 27.254 min, 4 Scans) Frag=175.0V CID@15.0 (317.1038[z=1] -> **) Bla…
x10 3
181.0513
137.0614
119.0488
93.0330
317.1113
Counts vs. Mass-to-Charge (m/z)

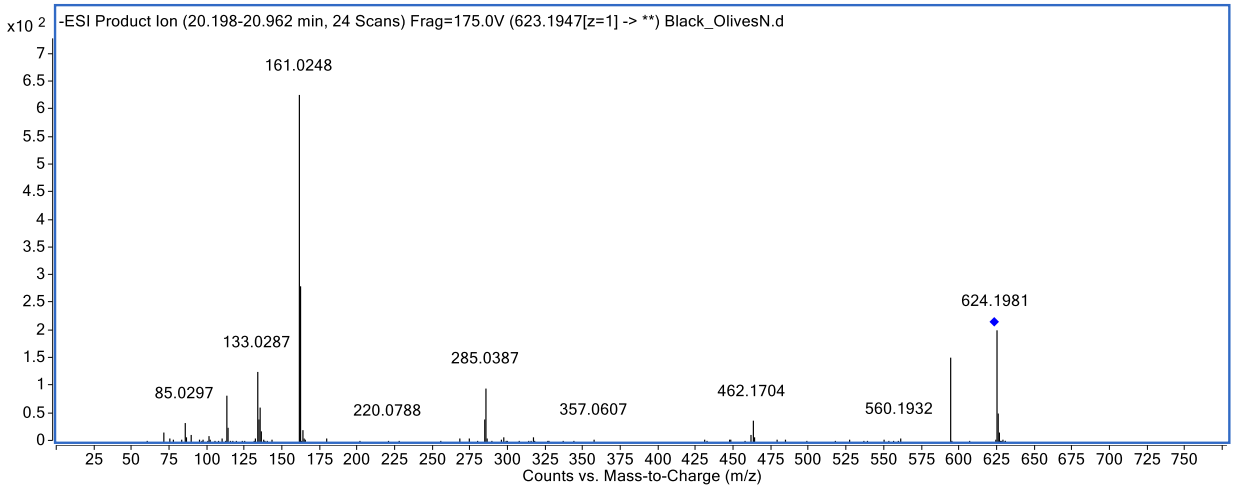

Hydroxytyrosol 4-O-glucoside: (M-H)-: -ESI Product Ion (34.206, 34.344, 34.398, 34.501 min, 4 Scans) Frag=175.0V CID@10.0 (315.1053[z=…
x10 3
315.1126
163.0347
145.0249
119.0430
93.0337
183.8732
227.1398
247.2632
273.7402
Counts vs. Mass-to-Charge (m/z)

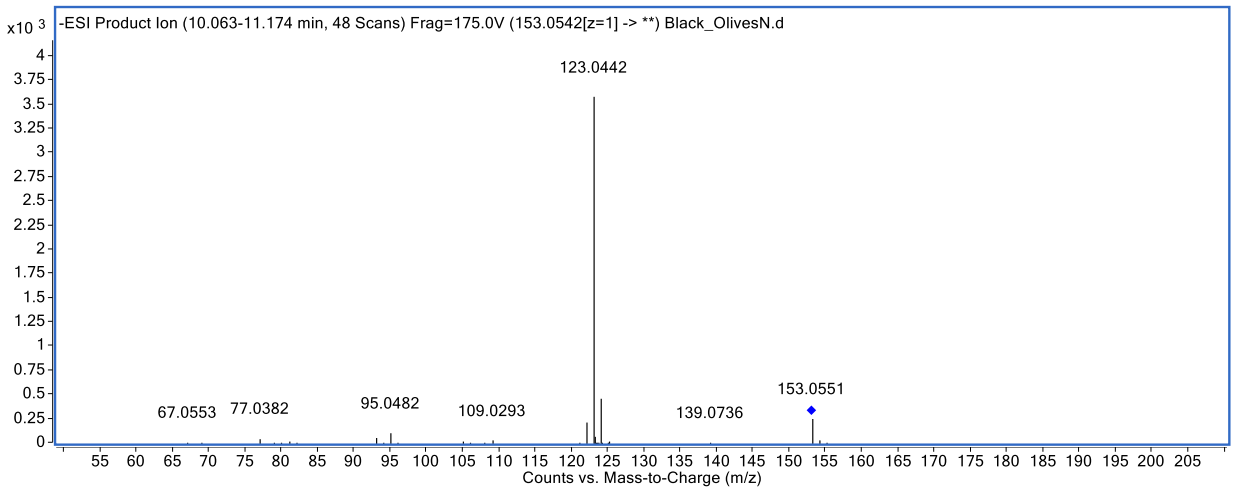




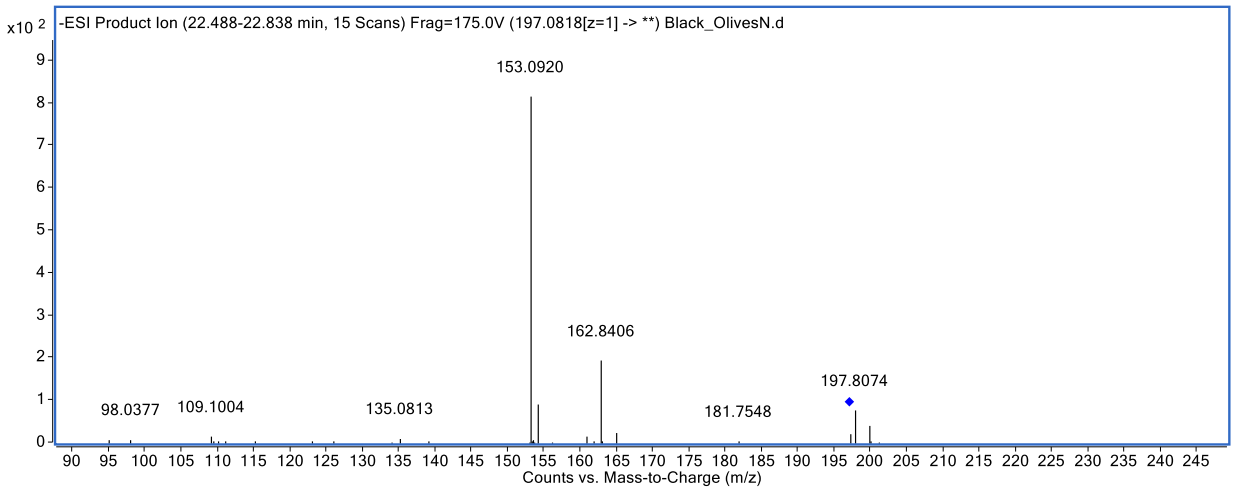
Vaccinoside


x10 3
-ESI Product Ion (23.685-24.286 min, 21 Scans) Frag=175.0V (535.1445[z=1] -> **) Black_OlivesN.d
145.0296
69.0356
117.0348
205.0494
266.0742
346.1214
390.1125
492.1524
536.1503
Counts vs. Mass-to-Charge (m/z)

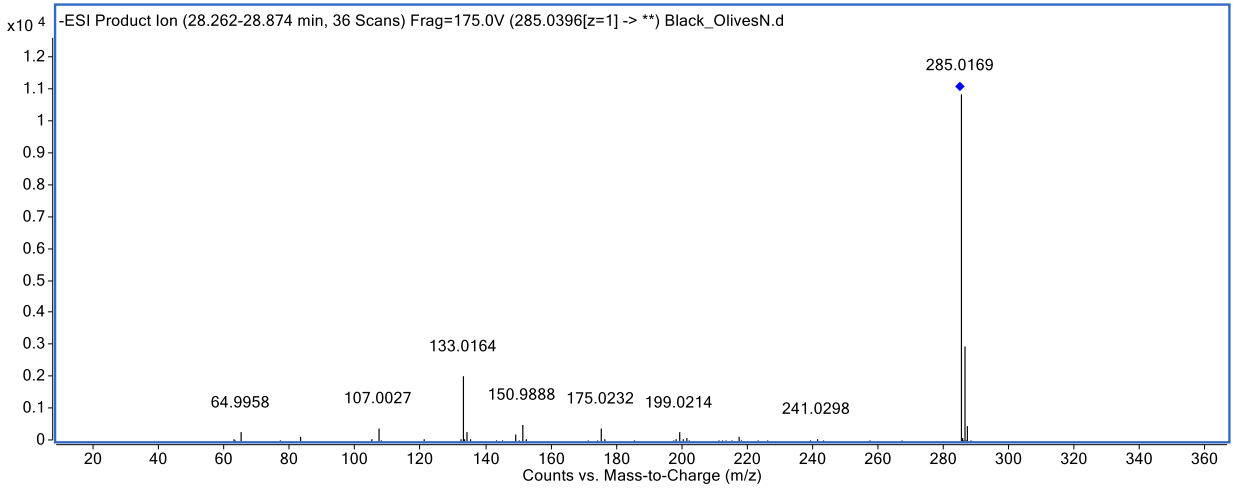

x10 2
-ESI Product Ion (20.198-20.962 min, 24 Scans) Frag=175.0V (623.1947[z=1] -> **) Black_OlivesN.d
161.0248
133.0287
85.0297
220.0788
285.0387
357.0607
462.1704
560.1932
624.1981
Counts vs. Mass-to-Charge (m/z)

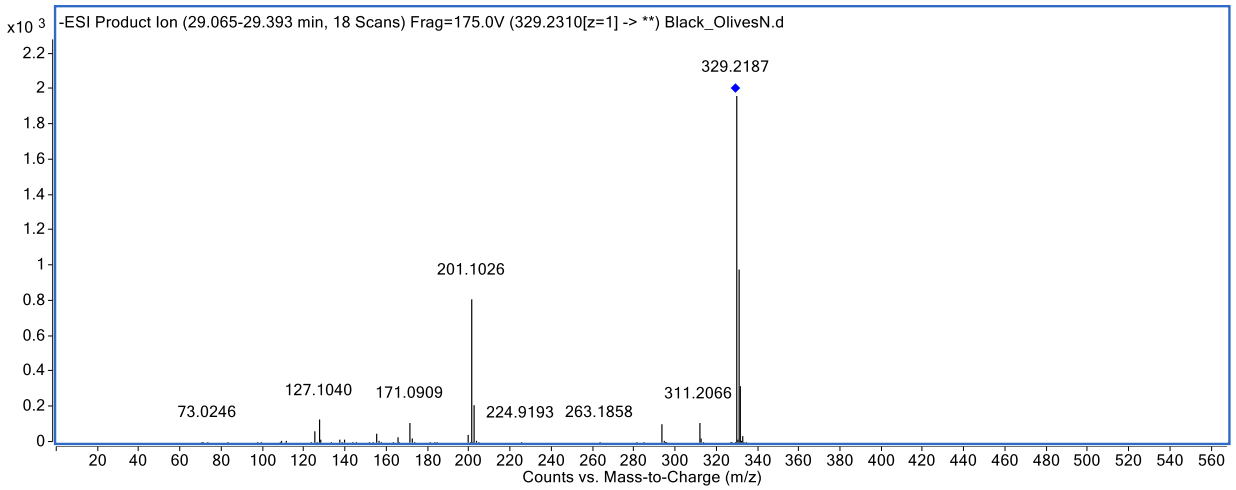


Syringic acid

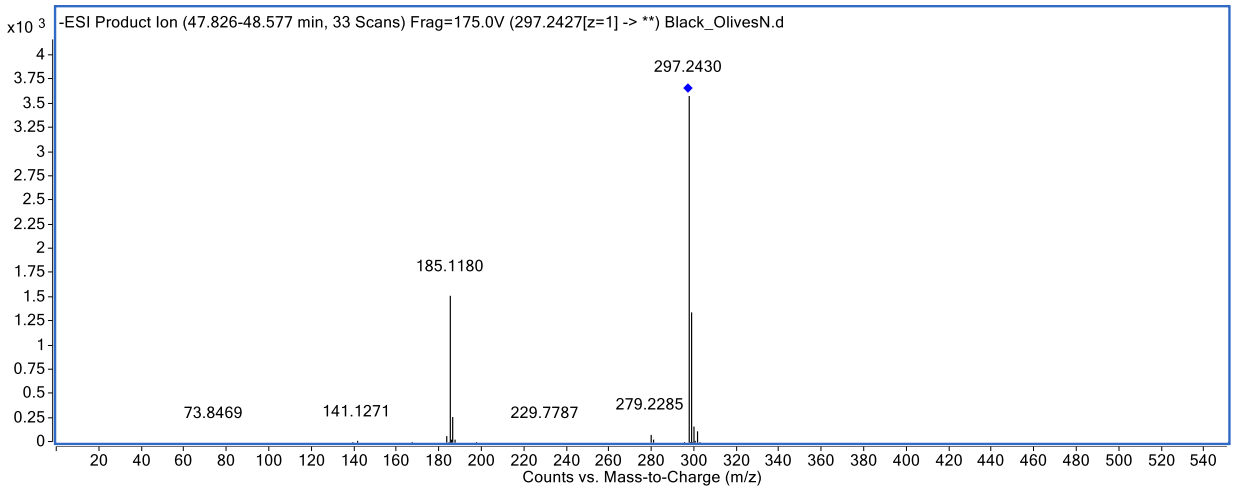


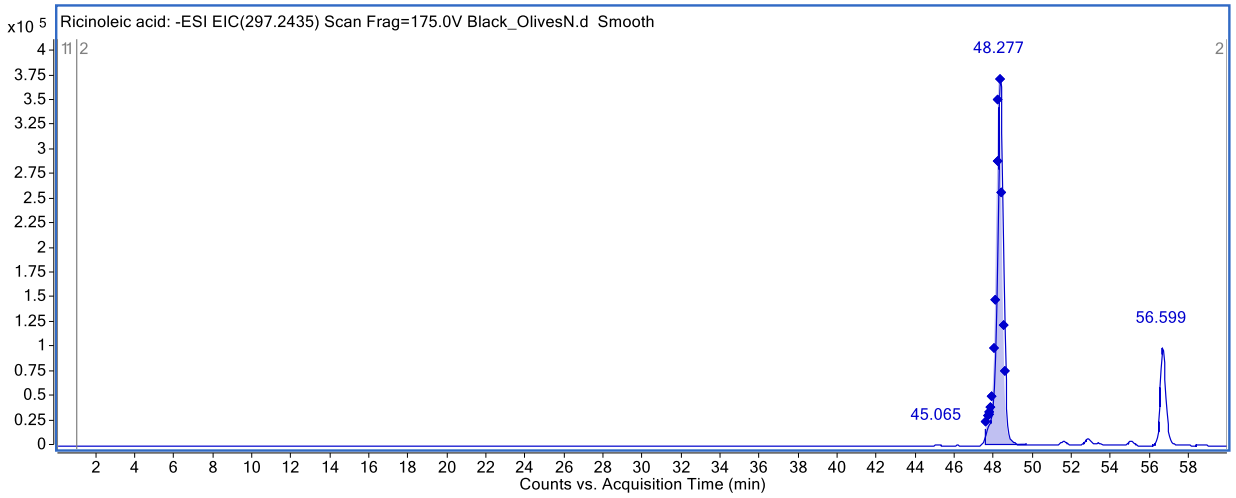
Luteolin


-ESI Product Ion (28.262-28.874 min, 36 Scans) Frag=175.0V (285.0396[z=1] -> **) Black_OlivesN.d
x10 4
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
285.0169
133.0164
64.9958
107.0027
150.9888
175.0232
199.0214
241.0298
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320
340
360
Counts vs. Mass-to-Charge (m/z)

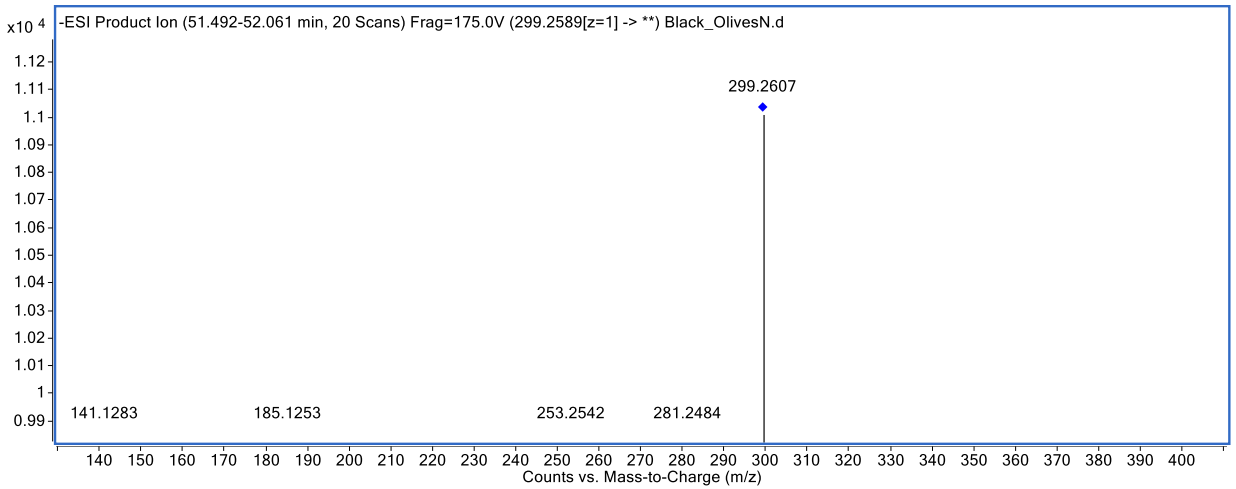


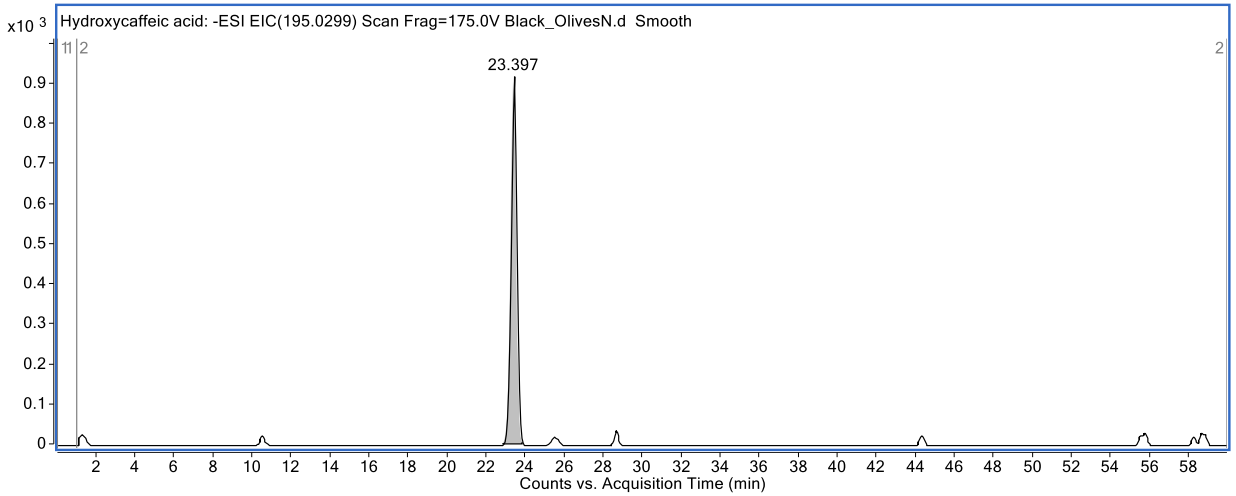
Ricinoleic acid

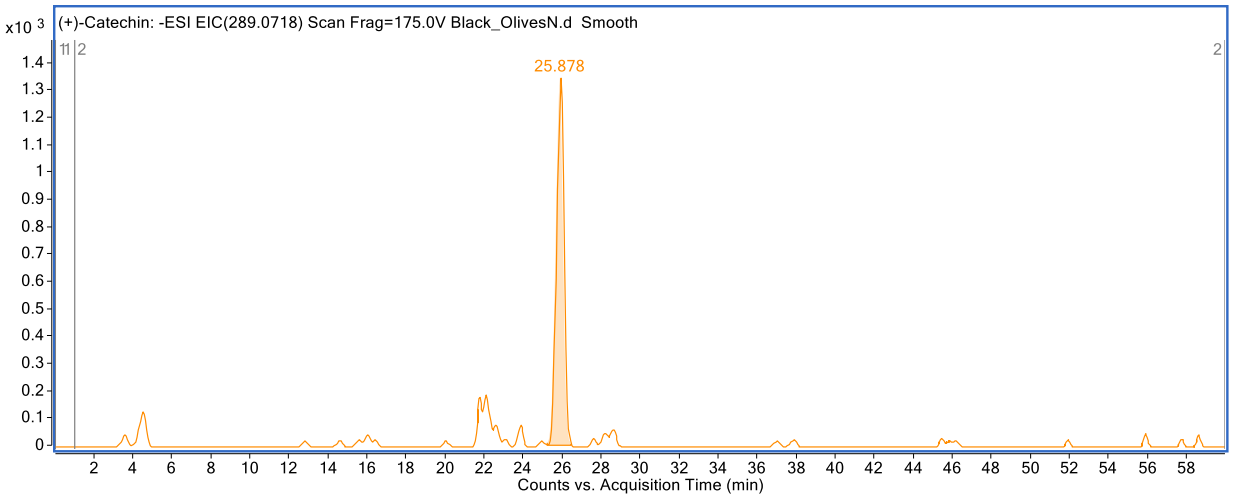


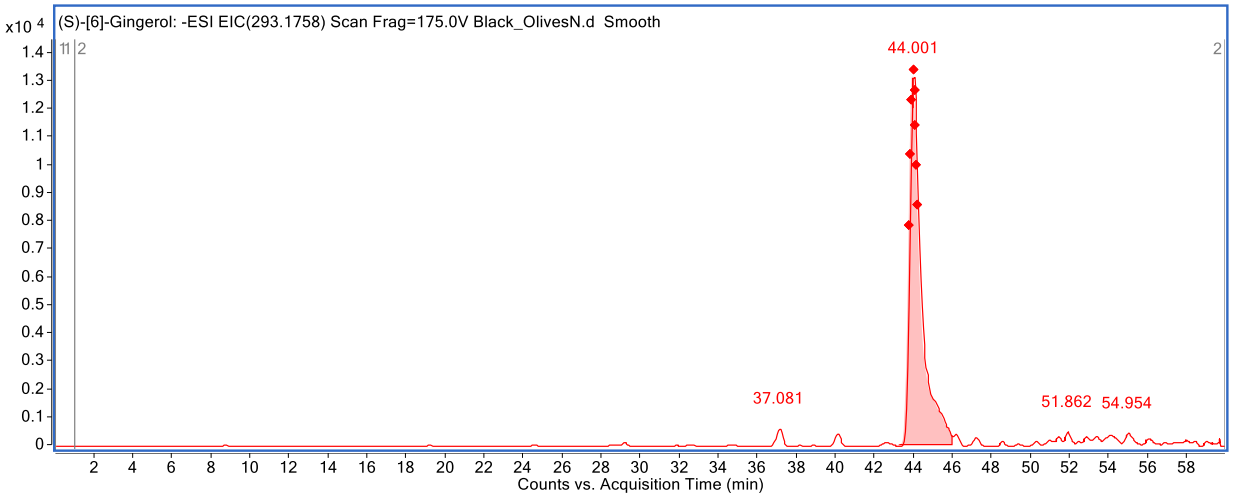


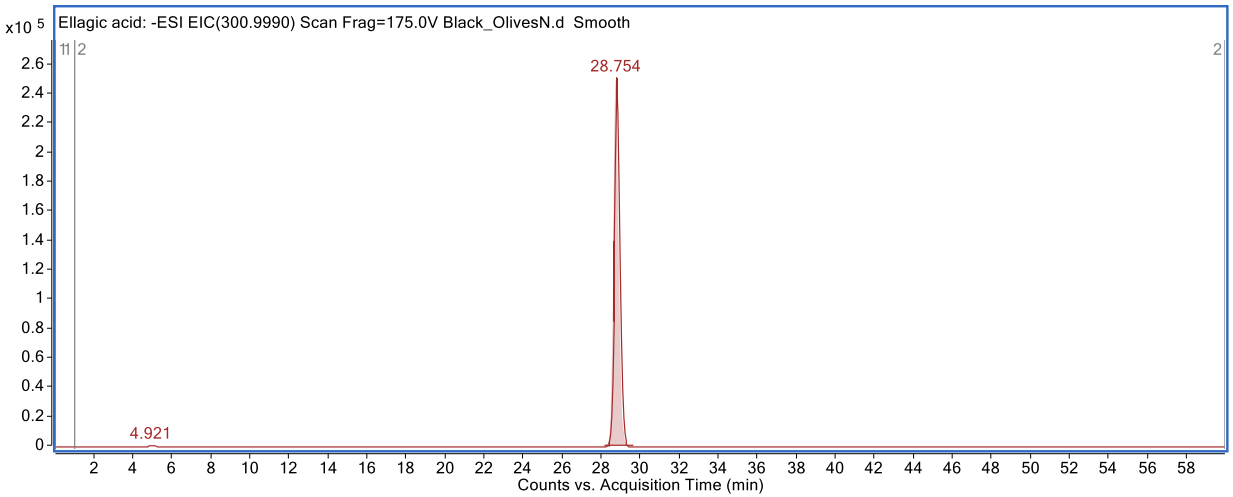
2-Hydroxystearic acid

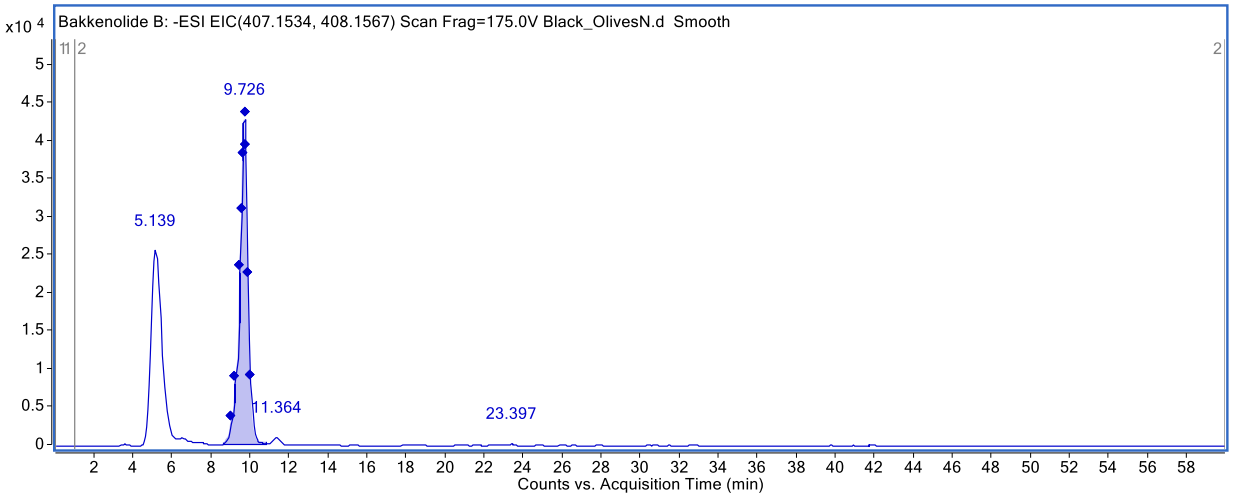

x10 4
-ESI Product Ion (51.492-52.061 min, 20 Scans) Frag=175.0V (299.2589[z=1] -> **) Black_OlivesN.d
299.2607
141.1283
185.1253
253.2542
281.2484
Counts vs. Mass-to-Charge (m/z)

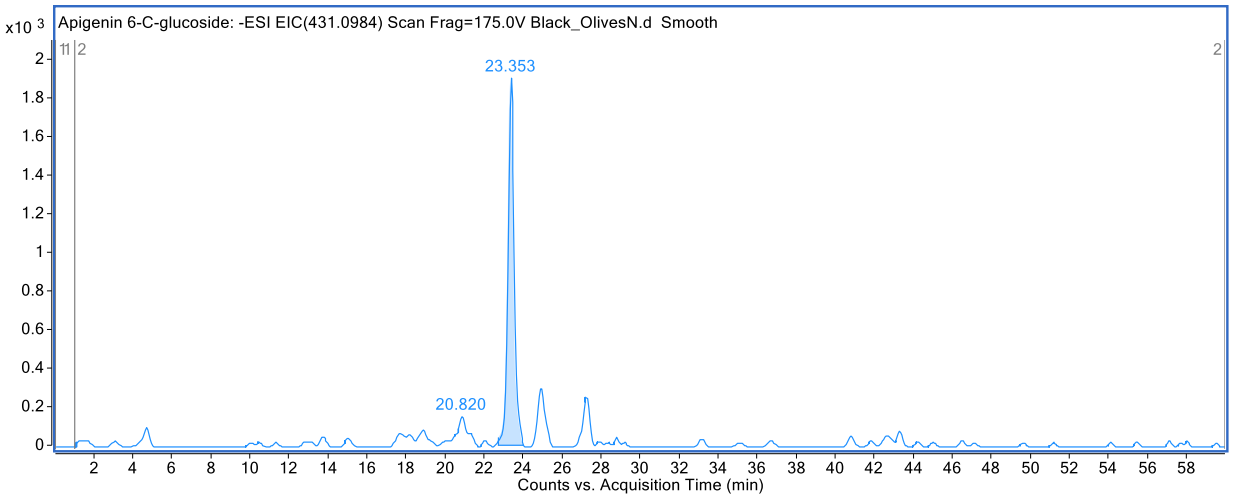

x10 3
Hydroxycaffeic acid: -ESI EIC(195.0299) Scan Frag=175.0V Black_OlivesN.d Smooth
23.397
Counts vs. Acquisition Time (min)

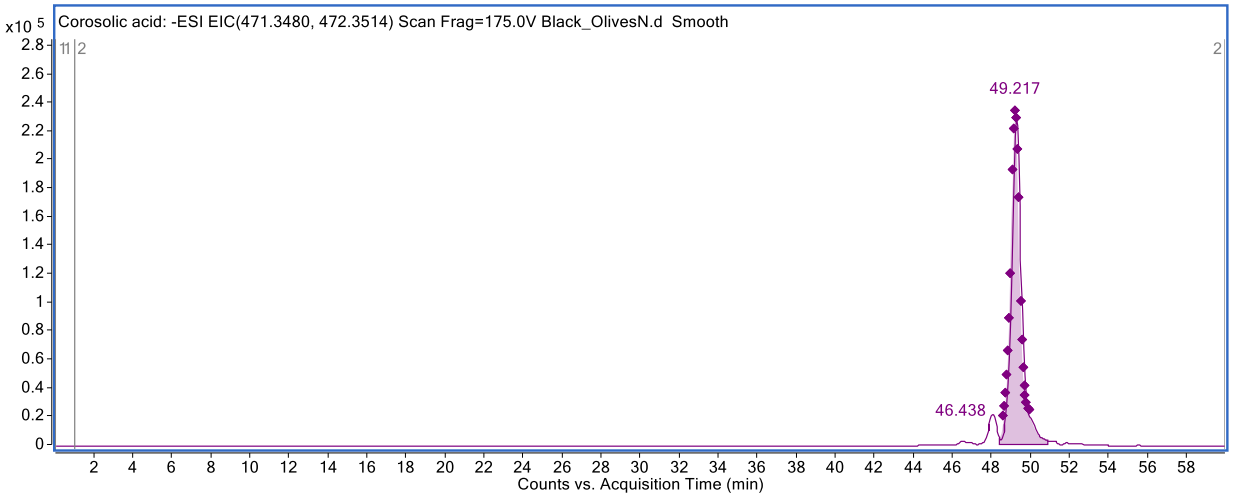

x10 3
(+)-Catechin: -ESI EIC(289.0718) Scan Frag=175.0V Black_OlivesN.d Smooth
25.878
Counts vs. Acquisition Time (min)


x10 4
(S)-[6]-Gingerol: -ESI EIC(293.1758) Scan Frag=175.0V Black_OlivesN.d Smooth
44.001
37.081
51.862
54.954
Counts vs. Acquisition Time (min)


x10 5
Ellagic acid: -ESI EIC(300.9990) Scan Frag=175.0V Black_OlivesN.d Smooth
28.754
4.921
Counts vs. Acquisition Time (min)


x10 4
Bakkenolide B: -ESI EIC(407.1534, 408.1567) Scan Frag=175.0V Black_OlivesN.d Smooth
9.726
5.139
11.364
23.397
Counts vs. Acquisition Time (min)


x10 3
Apigenin 6-C-glucoside: -ESI EIC(431.0984) Scan Frag=175.0V Black_OlivesN.d Smooth
11 2
2
23.353
20.820
Counts vs. Acquisition Time (min)


x10 5
Corosolic acid: -ESI EIC(471.3480, 472.3514) Scan Frag=175.0V Black_OlivesN.d Smooth
11 2
2
49.217
46.438
Counts vs. Acquisition Time (min)

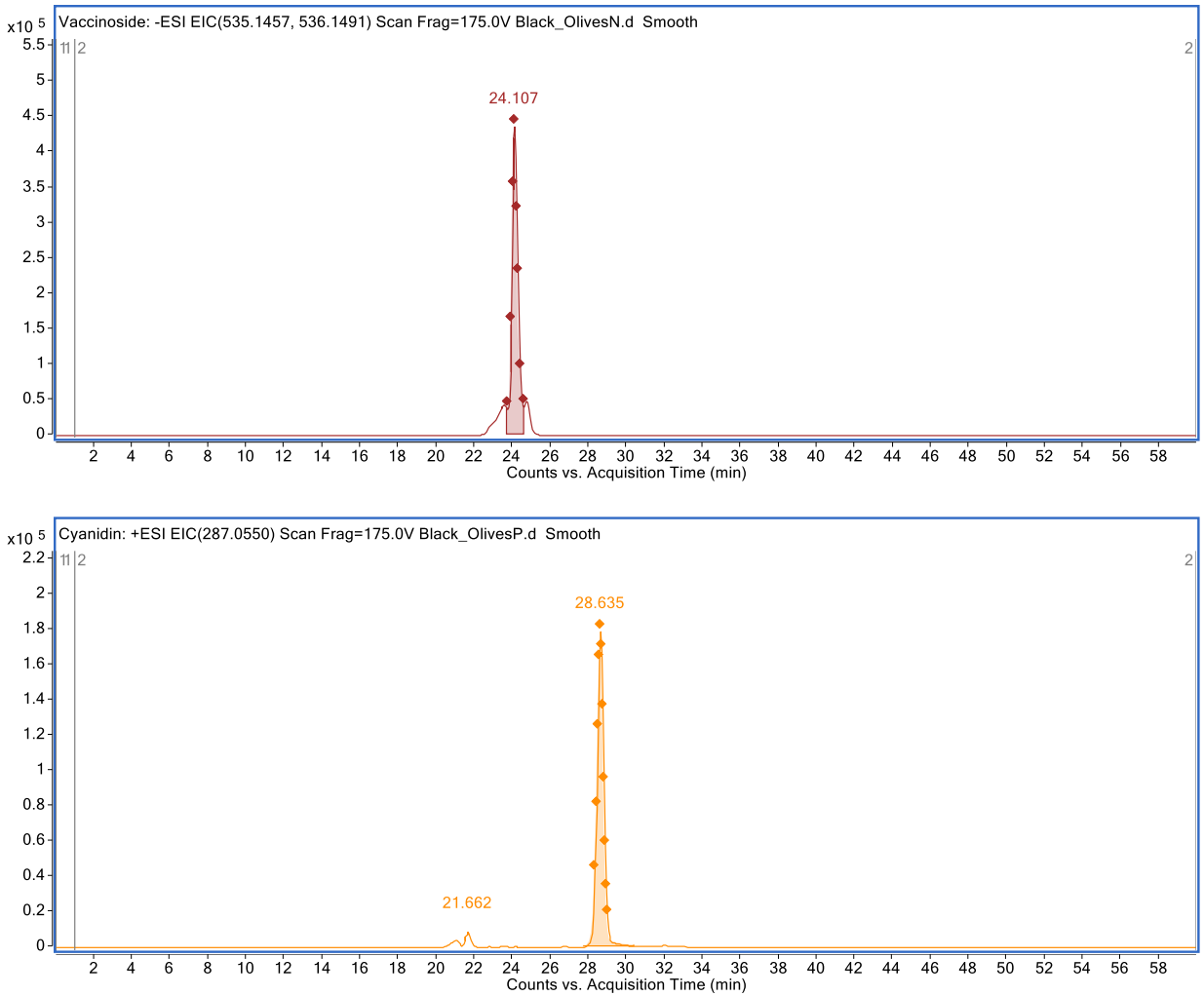


Figure S2. Chromatograms and MS/MS spectra of some selected compounds

Table S1. Radar bioavailability properties of selected compounds

No.	Compounds	MW	Rotatable bonds	XLOGP3	TPSA	WLOGP	ESOL Log S	Fraction Csp3	Lipinski violations	Bioavailability Score
1	3-p-Coumaroylquinic acid	338.31	5	-0.07	144.52	-0.46	-1.75	0.38	0	0.56
2	Caffeic acid	180.16	2	1.15	77.76	1.09	-1.89	0.00	0	0.56
3	Chlorogenic acid	354.31	5	-0.42	164.75	-0.75	-1.62	0.38	1	0.11
4	Cinnamic acid	148.16	2	2.13	37.30	1.68	-2.37	0.00	0	0.85
5	Ellagic acid	302.19	0	1.1	141.34	1.31	-2.94	0.00	0	0.55
6	Ferulic acid	194.18	3	1.51	66.76	1.39	-2.11	0.10	0	0.85
7	p-Coumaric acid	164.16	2	1.46	57.53	1.38	-2.02	0.00	0	0.85
8	p-Hydroxybenzoic acid	138.12	1	1.58	57.53	1.09	-2.07	0.00	0	0.85
9	Protocatechuic acid	154.12	1	1.15	77.76	0.80	-1.86	0.00	0	0.56
10	Quinic acid	192.17	1	-2.37	118.22	-2.32	0.53	0.86	0	0.56
11	Syringic acid	198.17	3	1.04	75.99	1.11	-1.84	0.22	0	0.56
12	Cyanidin	287.24	1	0.77	114.29	2.91	-2.6	0.00	0	0.55
13	Cyanidin 3-O-rutinoside	595.53	6	-2.68	252.36	-0.77	-1.73	0.44	3	0.17
14	Cyanidin 3-O-glucoside	449.38	4	0.14	193.44	0.38	-2.82	0.29	2	0.17
15	Delphinidin	303.24	1	0.41	134.52	2.61	-2.45	0.00	1	0.55
16	Chrysin	254.24	1	3.52	70.67	2.87	-4.19	0.00	0	0.55
17	Diosmin	608.54	7	0.14	238.20	-1.09	-3.51	0.46	3	0.17
18	Epicatechin	290.27	1	0.36	110.38	1.22	-2.22	0.20	0	0.55
19	Isorhamnetin	316.26	2	1.87	120.36	2.29	-3.36	0.06	0	0.55
20	Luteolin	286.24	1	2.53	111.13	2.28	-3.71	0.00	0	0.55
21	Naringin	580.53	6	-0.44	225.06	-1.49	-2.98	0.52	3	0.17
22	Quercetin	302.24	1	1.54	131.36	1.99	-3.16	0.00	0	0.55
23	Quercetin-3-glucoside	464.38	4	0.36	210.51	-0.54	-3.04	0.29	2	0.17
24	Taxifolin	304.25	1	0.95	127.45	0.86	-2.66	0.13	0	0.55
25	Rutin	610.52	6	-0.33	269.43	-1.69	-3.3	0.44	3	0.17
26	Coumarin	146.14	0	1.39	30.21	1.79	-2.29	0.00	0	0.55
27	Pyrogallol	126.11	0	0.52	60.69	0.80	-1.44	0.00	0	0.55
28	Corosolic acid	472.7	1	6.37	77.76	6.06	-6.72	0.90	1	0.56
29	Hesperidin	610.56	7	-0.14	234.29	-1.48	-3.28	0.54	3	0.17
30	Neoeriocitrin	596.53	6	-0.8	245.29	-1.78	-2.85	0.52	3	0.17
31	Tricin	330.29	3	3.07	109.36	2.59	-4.12	0.12	0	0.55
32	Quercitrin	448.38	3	0.86	190.28	0.49	-3.33	0.29	2	0.17
33	Naringenin	272.25	1	2.52	86.99	2.19	-3.49	0.13	0	0.55

34	Eriodictyol	288.25	1	2.02	107.22	1.89	-3.26	0.13	0	0.55
35	Linoleic acid	280.45	14	6.98	37.30	5.88	-5.05	0.72	1	0.85
36	Oleic acid	282.45	15	7.64	37.30	6.11	-5.41	0.83	1	0.85
37	Hydroxytyrosol 4-O-glucoside	316.3	5	-1.33	139.84	-1.89	-0.84	0.57	1	0.55
38	Melatonin	232.28	5	1.59	54.12	1.86	-2.34	0.31	0	0.55
39	Hydroxytyrosol	154.16	2	-0.72	60.69	0.63	-0.61	0.25	0	0.55

(Lipophilicity: XLOGP3 between −0.7 and +5.0, size: MW between 150 and 500 g/mol, polarity: TPSA between 20 and 130Å, solubility: log S not higher than 6, saturation: fraction of carbons in the sp3 hybridization not less than 0.25, and flexibility: no more than nine rotatable bonds; topological polar surface area (TPSA)

Table S2. Pharmacokinetics properties of selected compounds

No.	Molecule	GI absorption	BBB permeant	P-gp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	log Kp (cm/s) skin permeation
1	3-p-Coumaroylquinic acid	Low	No	No	No	No	No	No	No	-8.41
2	Caffeic acid	High	No	No	No	No	No	No	No	-6.58
3	Chlorogenic acid	Low	No	No	No	No	No	No	No	-8.76
4	Cinnamic acid	High	Yes	No	No	No	No	No	No	-5.69
5	Ellagic acid	High	No	No	Yes	No	No	No	No	-7.36
6	Ferulic acid	High	Yes	No	No	No	No	No	No	-6.41
7	p-Coumaric acid	High	Yes	No	No	No	No	No	No	-6.26
8	p-Hydroxybenzoic acid	High	Yes	No	No	No	No	No	No	-6.02
9	Protocatechuic acid	High	No	No	No	No	No	No	Yes	-6.42
10	Quinic acid	Low	No	Yes	No	No	No	No	No	-9.15
11	Syringic acid	High	No	No	No	No	No	No	No	-6.77
12	Cyanidin	High	No	Yes	Yes	No	No	No	No	-7.51
13	Cyanidin 3-O-rutinoside	Low	No	No	No	No	No	No	No	-11.84
14	Cyanidin 3-O-glucoside	Low	No	No	No	No	No	No	No	-8.94
15	Delphinidin	High	No	Yes	Yes	No	No	No	No	-7.86
16	Chrysin	High	Yes	No	Yes	No	No	Yes	Yes	-5.35
17	Diosmin	Low	No	Yes	No	No	No	No	No	-9.91
18	Epicatechin	High	No	Yes	No	No	No	No	No	-7.82
19	Isorhamnetin	High	No	No	Yes	No	No	Yes	Yes	-6.9
20	Luteolin	High	No	No	Yes	No	No	Yes	Yes	-6.25
21	Naringin	Low	No	Yes	No	No	No	No	No	-10.15
22	Quercetin	High	No	No	Yes	No	No	Yes	Yes	-7.05
23	Quercetin-3-glucoside	Low	No	No	No	No	No	No	No	-8.88
24	Taxifolin	High	No	No	No	No	No	No	No	-7.48
25	Rutin	Low	No	Yes	No	No	No	No	No	-10.26
26	Coumarin	High	Yes	No	Yes	No	No	No	No	-6.2
27	Pyrogallol	High	Yes	No	No	No	No	No	Yes	-6.7
28	Corosolic acid	High	No	Yes	No	No	No	No	No	-4.66
29	Hesperidin	Low	No	Yes	No	No	No	No	No	-10.12
30	Neoeriocitrin	Low	No	Yes	No	No	No	No	No	-10.51
31	Tricin	High	No	No	Yes	No	Yes	Yes	Yes	-6.14
32	Quercitrin	Low	No	No	No	No	No	No	No	-8.42
33	Naringenin	High	No	Yes	Yes	No	No	No	Yes	-6.17
34	Eriodictyol	High	No	Yes	No	No	No	No	Yes	-6.62

35	Linoleic acid	High	Yes	No	Yes	No	Yes	No	No	-3.05
36	Oleic acid	High	No	No	Yes	No	Yes	No	No	-2.6
37	Hydroxytyrosol 4-O-glucoside	Low	No	No	No	No	No	No	No	-9.17
38	Melatonin	High	Yes	No	Yes	No	No	No	No	-6.59
39	Hydroxytyrosol	High	No	No	No	No	No	No	No	-7.75

Table S3. Predicted absorption and distribution of selected compounds.

		Absorption						Distribution				
No.	Compounds	Water solubility	Caco2 permeability	Intestinal absorption (human)	Skin Permeability	P-g substrate	P-g I inhibitor	P-g II inhibitor	VDss (human)	Fraction unbound (human)	BBB permeability	CNS permeability
1	3-*p*-Coumaroylquinic acid	-1.99	-0.66	43.93	-2.74	Yes	No	No	0.03	0.61	-1.16	-3.69
2	Caffeic acid	-2.33	0.63	69.41	-2.72	No	No	No	-1.10	0.53	-0.65	-2.61
3	Chlorogenic acid	-2.45	-0.84	36.38	-2.74	Yes	No	No	0.58	0.66	-1.41	-3.86
4	Cinnamic acid	-2.61	1.72	94.83	-2.70	No	No	No	-1.05	0.38	0.45	-1.83
5	Ellagic acid	-3.18	0.34	86.68	-2.74	Yes	No	No	0.38	0.08	-1.27	-3.53
6	Ferulic acid	-2.82	0.18	93.69	-2.72	No	No	No	-1.37	0.34	-0.24	-2.61
7	p-Coumaric acid	-2.38	1.21	93.49	-2.72	No	No	No	-1.15	0.43	-0.23	-2.42
8	p-Hydroxybenzoic acid	-1.88	1.15	83.96	-2.72	No	No	No	-1.56	0.59	-0.33	-3.21
9	Protocatechuic acid	-2.07	0.49	71.17	-2.73	No	No	No	-1.30	0.65	-0.68	-3.31
10	Quinic acid	-1.12	-0.26	32.27	-2.74	No	No	No	-0.22	0.82	-0.89	-3.67
11	Syringic acid	-2.22	0.50	73.08	-2.74	Yes	No	No	-1.44	0.60	-0.19	-2.70
12	Cyanidin	-2.94	-0.35	87.30	-2.74	Yes	No	No	0.95	0.24	-1.23	-2.22
13	Cyanidin 3-O-rutinoside	-2.89	-1.09	23.05	-2.74	Yes	No	Yes	1.94	0.18	-2.15	-4.94
14	Cyanidin 3-O-glucoside	-2.93	0.06	45.39	-2.74	Yes	No	No	1.46	0.27	-1.71	-3.81
15	Delphinidin	-2.92	-0.83	77.39	-2.74	Yes	No	No	0.86	0.31	-1.62	-3.52
16	Chrysin	-3.54	0.95	93.76	-2.74	Yes	No	No	0.40	0.14	0.05	-1.91
17	Diosmin	-2.93	0.31	29.32	-2.74	Yes	No	No	1.43	0.11	-1.80	-4.84
18	Epicatechin	-3.12	-0.28	68.83	-2.74	Yes	No	No	1.03	0.24	-1.05	-3.30
19	Isorhamnetin	-3.00	0.00	76.01	-2.74	Yes	No	No	1.12	0.09	-1.14	-3.19
20	Luteolin	-3.09	0.10	81.13	-2.74	Yes	No	No	1.15	0.17	-0.91	-2.25
21	Naringin	-2.92	-0.66	25.80	-2.74	Yes	No	No	0.62	0.16	-1.60	-4.77
22	Quercetin	-2.93	-0.23	77.21	-2.74	Yes	No	No	1.56	0.21	-1.10	-3.07
23	Quercetin-3-glucoside	-2.93	0.24	48.00	-2.74	Yes	No	No	1.85	0.23	-1.69	-4.09
24	Taxifolin	-3.04	0.92	64.71	-2.74	Yes	No	No	1.64	0.32	-0.73	-3.20
25	Rutin	-2.89	-0.95	23.45	-2.74	Yes	No	No	1.66	0.19	-1.90	-5.18
26	Coumarin	-1.52	1.65	97.34	-1.92	No	No	No	-0.14	0.37	-0.01	-1.93
27	Pyrogallol	-1.41	1.12	83.55	-2.75	No	No	No	0.13	0.71	-0.44	-3.25
28	Corosolic acid	-3.04	0.64	100.00	-2.74	No	No	No	-1.28	0.04	-0.47	-1.51
29	Hesperidin	-3.01	0.51	31.48	-2.74	Yes	No	No	1.00	0.10	-1.72	-4.81
30	Neoeriocitrin	-2.90	-0.86	16.14	-2.74	Yes	No	No	0.83	0.18	-1.84	-4.93

31	Tricin	-3.28	0.12	89.71	-2.74	Yes	No	No	0.80	0.08	-1.12	-3.41
32	Quercitrin	-2.90	0.05	52.71	-2.74	Yes	No	No	1.52	0.13	-1.50	-4.16
33	Naringenin	-3.22	1.03	91.31	-2.74	Yes	No	No	-0.02	0.06	-0.58	-2.22
34	Eriodictyol	-3.25	-0.09	74.69	-2.74	Yes	No	No	0.38	0.11	-0.83	-3.14
35	Linoleic acid	-5.86	1.57	92.33	-2.72	No	No	No	-0.59	0.05	-0.14	-1.60
36	Oleic acid	-5.9	1.56	91.83	-2.72	No	No	No	-0.59	0.05	-0.17	-1.65
37	Hydroxytyrosol 4-O-glucoside	-1.52	0.05	38.53	-2.73	No	No	No	-0.31	0.73	-1.15	-4.10
38	Melatonin	-2.47	1.22	94.16	-2.83	Yes	No	No	0.08	0.29	-0.08	-2.45
39	Hydroxytyrosol	-1.14	1.10	72.81	-2.89	No	No	No	-0.08	0.59	-0.39	-2.67

Intestinal absorption (human) (IA), P-glycoprotein substrate, P-glycoprotein I inhibitor, P-glycoprotein II inhibitor, Water solubility (log mol/L) (WS), Volume of distributions (VDss); blood-brain barrier (BBB); central nervous system (CNS)

Interpretation of results: If the Caco2 permeability value is higher than 0.90, a compound has a high Caco-2 permeability. A compound with a value of less than 30% is poorly absorbed in the human intestinal. If a compound has a value less than −2.5 is considered to have a low skin permeability. The compounds with values < −3 cannot penetrate the central nervous system, while values > −2 are considered to penetrate the central nervous system. The compounds with values logBB < −1 are poorly distributed to the brain while values logBB > 0.3 are considered to cross the blood-brain barrier readily. VDss is considered low if below 0.71 L/kg (log VDss < −0.15) and high if above 2.81 L/kg (log VDss > 0.45).

Table S4. Predicted metabolism and excretion of selected compounds.

		Metabolism							Excretion	
No.	Compounds	CYP2D6 substrate	CYP3A4 substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Total Clearance	Renal OCT2 substrate
1	3-p-Coumaroylquinic acid	No	No	No	No	No	No	No	0.45	No
2	Caffeic acid	No	No	No	No	No	No	No	0.51	No
3	Chlorogenic acid	No	No	No	No	No	No	No	0.31	No
4	Cinnamic acid	No	No	No	No	No	No	No	0.78	No
5	Ellagic acid	No	No	Yes	No	No	No	No	0.54	No
6	Ferulic acid	No	No	No	No	No	No	No	0.62	No
7	p-Coumaric acid	No	No	No	No	No	No	No	0.66	No
8	p-Hydroxybenzoic acid	No	No	No	No	No	No	No	0.59	No
9	Protocatechuic acid	No	No	No	No	No	No	No	0.55	No
10	Quinic acid	No	No	No	No	No	No	No	0.64	No
11	Syringic acid	No	No	No	No	No	No	No	0.65	No
12	Cyanidin	No	No	Yes	No	No	No	No	0.53	No
13	Cyanidin 3-O-rutinoside	No	No	No	No	No	No	No	-0.27	No
14	Cyanidin 3-O-glucoside	No	No	No	No	No	No	No	0.52	No
15	Delphinidin	No	No	Yes	No	No	No	No	0.58	No
16	Chrysin	No	No	Yes	Yes	Yes	No	No	0.41	No
17	Diosmin	No	No	No	No	No	No	No	-0.11	No
18	Epicatechin	No	No	No	No	No	No	No	0.18	No
19	Isorhamnetin	No	No	Yes	No	No	No	No	0.51	No
20	Luteolin	No	No	Yes	No	Yes	No	No	0.50	No
21	Naringin	No	No	No	No	No	No	No	0.32	No
22	Quercetin	No	No	Yes	No	No	No	No	0.41	No
23	Quercetin-3-glucoside	No	No	No	No	No	No	No	0.39	No
24	Taxifolin	No	No	No	No	No	No	No	-0.08	No
25	Rutin	No	No	No	No	No	No	No	-0.37	No
26	Coumarin	No	No	Yes	No	No	No	No	0.97	No
27	Pyrogallol	No	No	No	No	No	No	No	0.10	No
28	Corosolic acid	No	Yes	No	No	No	No	No	0.09	No
29	Hesperidin	No	No	No	No	No	No	No	0.21	No
30	Neoeriocitrin	No	No	No	No	No	No	No	0.13	No
31	Tricin	No	No	Yes	Yes	No	No	No	0.62	No
32	Quercitrin	No	No	No	No	No	No	No	0.36	No

33	Naringenin	No	No	Yes	No	No	No	No	0.06	No
34	Eriodictyol	No	No	No	No	No	No	No	-0.01	No
35	Linoleic acid	No	Yes	Yes	No	No	No	No	1.94	No
36	Oleic acid	No	Yes	Yes	No	No	No	No	1.89	No
37	Hydroxytyrosol 4-O-glucoside	No	No	No	No	No	No	No	0.21	No
38	Melatonin	No	No	Yes	No	No	No	No	0.74	No
39	Hydroxytyrosol	No	No	No	No	No	No	No	0.23	No

Organic cation transporter 2 (OCT2)

Table S5. Predicted toxicity of abundant phenolic compounds

No.	Compounds	AMES toxicity	MTD-H	hERG I inhibitor	hERG II inhibitor	ORAT (LD50)	LOAEL	Hepatotoxicity	Skin Sensitization	*T. pyriformis* toxicity	Minnow toxicity
1	3-*p*-Coumaroylquinic acid	No	-0.09	No	No	1.74	2.51	No	No	0.29	4.61
2	Caffeic acid	No	1.15	No	No	2.38	2.09	No	No	0.29	2.25
3	Chlorogenic acid	No	-0.13	No	No	1.97	2.98	No	No	0.29	5.74
4	Cinnamic acid	No	1.11	No	No	2.09	2.65	No	No	0.25	1.72
5	Ellagic acid	No	0.48	No	No	2.40	2.70	No	No	0.30	2.11
6	Ferulic acid	No	1.08	No	No	2.28	2.07	No	No	0.27	1.83
7	p-Coumaric acid	No	1.11	No	No	2.16	2.53	No	No	0.32	1.61
8	p-Hydroxybenzoic acid	No	0.85	No	No	2.26	2.48	No	No	0.27	1.81
9	Protocatechuic acid	No	0.81	No	No	2.42	2.02	No	No	0.27	2.45
10	Quinic acid	No	1.63	No	No	1.13	3.53	No	No	0.29	4.87
11	Syringic acid	No	1.37	No	No	2.16	2.42	No	No	0.28	2.55
12	Cyanidin	No	0.50	No	No	2.46	2.54	No	No	0.29	2.55
13	Cyanidin 3-O-rutinoside	No	0.46	No	Yes	2.50	3.29	No	No	0.29	5.70
14	Cyanidin 3-O-glucoside	No	0.56	No	Yes	2.55	4.20	No	No	0.29	6.40
15	Delphinidin	No	0.51	No	No	2.55	2.93	No	No	0.29	3.31
16	Chrysin	No	0.02	No	No	2.29	0.96	No	No	0.54	1.75
17	Diosmin	No	0.57	No	Yes	2.51	3.34	No	No	0.29	5.35
18	Epicatechin	No	0.44	No	No	2.43	2.50	No	No	0.35	3.59
19	Isorhamnetin	No	0.58	No	No	2.41	2.50	No	No	0.30	2.21
20	Luteolin	No	0.50	No	No	2.46	2.41	No	No	0.33	3.17

21	Naringin	No	0.43	No	Yes	2.50	4.20	No	No	0.29	6.04
22	Quercetin	No	0.50	No	No	2.47	2.61	No	No	0.29	3.72
23	Quercetin-3-glucoside	No	0.57	No	Yes	2.54	4.42	No	No	0.29	8.06
24	Taxifolin	No	0.35	No	No	2.26	3.10	No	No	0.29	4.69
25	Rutin	No	0.45	No	Yes	2.49	3.67	No	No	0.29	7.68
26	Coumarin	No	0.44	No	No	2.11	1.90	No	No	0.37	1.56
27	Pyrogallol	No	-0.27	No	No	2.05	2.37	No	No	0.13	2.73
28	Corosolic acid	No	0.12	No	No	2.51	1.86	Yes	No	0.29	0.28
29	Hesperidin	No	0.53	No	Yes	2.51	3.17	No	No	0.29	7.13
30	Neoeriocitrin	No	0.48	No	Yes	2.49	4.39	No	No	0.29	6.98
31	Tricin	No	0.35	No	No	2.23	1.82	No	No	0.33	1.75
32	Quercitrin	No	0.50	No	No	2.59	3.02	No	No	0.29	4.95
33	Naringenin	No	-0.18	No	No	1.79	1.94	No	No	0.37	2.14
34	Eriodictyol	No	0.01	No	No	2.03	2.48	No	No	0.33	2.97
35	Linoleic acid	No	-0.83	No	No	1.43	3.19	Yes	Yes	0.70	-1.31
36	Oleic acid	No	-0.81	No	No	1.42	3.23	No	Yes	0.68	-1.44
37	Hydroxytyrosol 4-O-glucoside	Yes	0.70	No	No	2.11	3.65	No	No	0.29	5.33
38	Melatonin	No	0.15	No	No	2.16	2.45	No	No	0.75	1.41
39	Hydroxytyrosol	Yes	1.15	No	No	1.86	1.91	No	No	-0.13	2.75

Oral Rat Acute Toxicity (ORAT), Oral Rat Chronic Toxicity (LOAEL), Max. tolerated dose (human) (MTD-H)

Explanations

Minnow toxicity

LC50 values below 0.5mM (log LC50 < −0.3) are regarded as high acute toxicity.

T. Pyriformis toxicity

pIGC50 (negative logarithm of the concentration required to inhibit 50% growth in log μg/L) is considered, with a value > −0.5 log μg/L is considered toxic.

AMES toxicity: if the AMES value is positive, the compound will be mutagenic.

Maximum tolerated dose: a value less than is equal to 0.477 log(mg/kg/day) is considered low and high if greater than 0.477 log(mg/kg/day).