Table S1. UPLC–MS/MS conditions for simultaneous analysis of the 14 marker components in GSH samples.

UPLC conditions		**MS/MS conditions**	
LC system	Acquity UPLC H-Class	MS system	Xevo TQ-S micro
Column	Acquity UPLC BEH C_{18} column (2.1 mm × 100 mm, 1.7 μm)	MS software	MassLynx (version 4.2)
Column temperature	40 °C	Ionization source	ESI
Sample temperature	5 °C	Ionization mode	Positive/Negative
Injection volume	2.0 μL	Acquisition mode	MRM
Flow rate	0.3 mL/min	Capillary voltage	3.3 kV
Mobile phase A	0.1% (v/v) Acetic acid in distilled water	Cone gas flow	80 L/h
Mobile phase B	0.1% (v/v) Acetic acid in acetonitrile	Desolvation gas flow	600 L/h
Gradient elution	Time (min) / A (%) / B (%) 0.00 / 95 / 5 11.43 / 40 / 60 14.29 / 5 / 95 15.71 / 5 / 95 17.14 / 95 / 5 20.00 / 95 / 5	Desolvation temperature	300 °C
		Source temperature	150 °C

Table S2. Repeatability of retention time of the 14 marker analytes in the developed UPLC–MS/MS MRM assay (n = 6).

Analyte	Retention time						Mean	SD	CV (%)
	1	2	3	4	5	6			
1	0.79	0.79	0.80	0.79	0.79	0.80	0.79	0.01	0.65
2	1.43	1.46	1.48	1.48	1.49	1.49	1.47	0.02	1.57
3	2.15	2.18	2.19	2.21	2.21	2.21	2.19	0.02	1.10
4	2.43	2.47	2.47	2.50	2.50	2.50	2.48	0.03	1.12
5	3.48	3.52	3.53	3.55	3.55	3.54	3.53	0.03	0.75
6	4.14	4.16	4.17	4.18	4.18	4.17	4.17	0.02	0.36
7	4.17	4.19	4.20	4.21	4.21	4.21	4.20	0.02	0.38
8	4.72	4.75	4.76	4.77	4.77	4.76	4.76	0.02	0.39
9	5.25	5.25	5.25	5.25	5.26	5.25	5.25	0.00	0.08
10	5.29	5.32	5.33	5.33	5.33	5.33	5.32	0.02	0.30
11	5.89	5.91	5.92	5.93	5.92	5.93	5.92	0.02	0.25
12	7.98	7.99	7.99	7.99	7.99	7.99	7.99	0.00	0.05
13	8.92	8.98	9.00	9.00	9.00	9.00	8.98	0.03	0.36
14	15.52	15.53	15.53	15.53	15.53	15.53	15.53	0.00	0.03

Allantoin (**1**), gallic acid (**2**), 5-(hydroxymethyl)furfural (**3**), geniposidic acid (**4**), oxypaeoniflorin (**5**), loganin (**6**), geniposide (**7**), paeoniflorin (**8**), ecdysterone (**9**), verbascoside (**10**), cornuside (**11**), benzoylpaeoniflorin (**12**), paeonol (**13**), and alisol B acetate (**14**).

Table S3. Composition of GSH.

Botanical name	Scientific name	Family	Used part	Origin	Amount (g)	Ratio (%)
Rehmanniae Radix Preparata	*Rehmannia glutinosa* (Gaertn.) DC.	Plantaginaceae	Root	Jeongeup, Korea	1481.4	29.7
Dioscoreae Rhizoma	*Dioscorea japonica* Thunb.	Dioscoreaceae	Rhizome	Korea	740.7	14.8
Corni Fructus	*Cornus officinalis* Siebold & Zucc.	Cornaceae	Fruit	Gurye, Korea	740.7	14.8
Poria Sclerotium	*Poria cocos* Wolf	Polyporaceae	Sclerotium	Binghwa, Korea	555.6	11.1
Moutan Radicis Cortex	*Paeonia suffruticosa* Andrews	Paeoniaceae	Root bark	Imsil, Korea	555.6	11.1
Alisamatis Rhizoma	*Alisma plantago-aquatica* subsp. *orientale* (Sam.) Sam.	Alismataceae	Rhizome	Imsil, Korea	555.6	11.1
Achyranthis Radix	*Achyranthes bidentate* Blume	Amaranthaceae	Root	Hwasun, Korea	185.2	3.7
Plantaginis Semen	*Plantago asiatica* L.	Plantaginaceae	Seed	China	185.2	3.7
				Total	5000.0	100.0

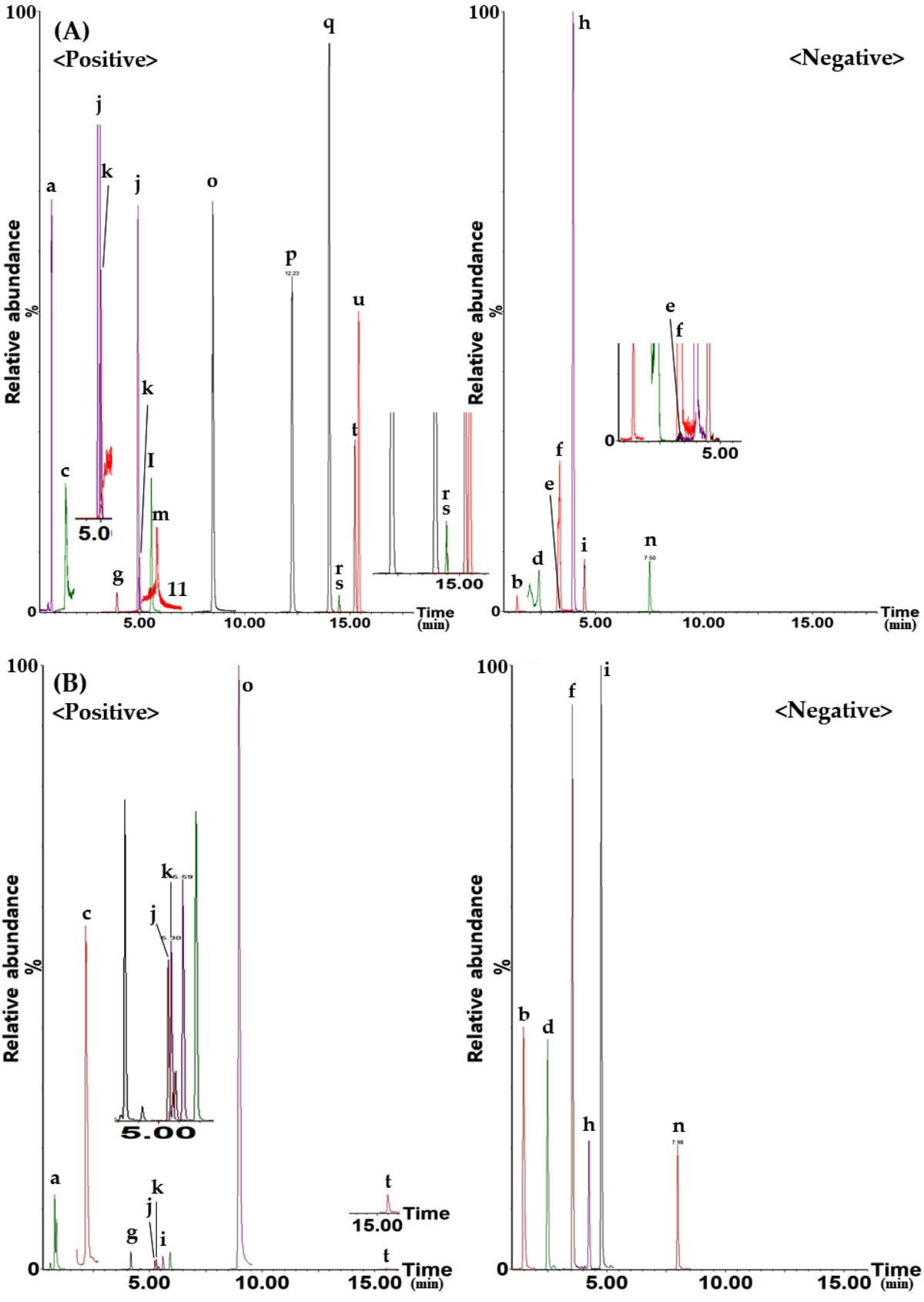

(A)
<Positive>
<Negative>
(B)
<Positive>
<Negative>
Relative abundance
%
Time
(min)
100
0
5.00
10.00
15.00
a
b
c
d
e
f
g
h
i
j
k
l
m
n
o
p
q
r
s
t
u
11

Figure S1. Total ion chromatograms of the 21 investigated standard component mixtures (A) and GSH sample (B) obtained using the UPLC–MS/MS MRM method in the positive and negative ion modes. Allantoin (**a**), gallic acid (**b**), 5-(hydroxymethyl)furfural (**c**), geniposidic acid (**d**), morroniside (**e**), oxypaeoniflorin (**f**), loganin (**g**), geniposide (**h**), paeoniflorin (**i**), ecdysterone (**j**), verbascoside (**k**), cornuside (**l**), benzoic acid (**m**), benzoylpaeoniflorin (**n**), paeonol (**o**), dioscin (**p**), polyporenic acid C (**q**), sweroside (**r**), alisol B (**s**), alisol B acetate (**t**), and pachymic acid (**u**).

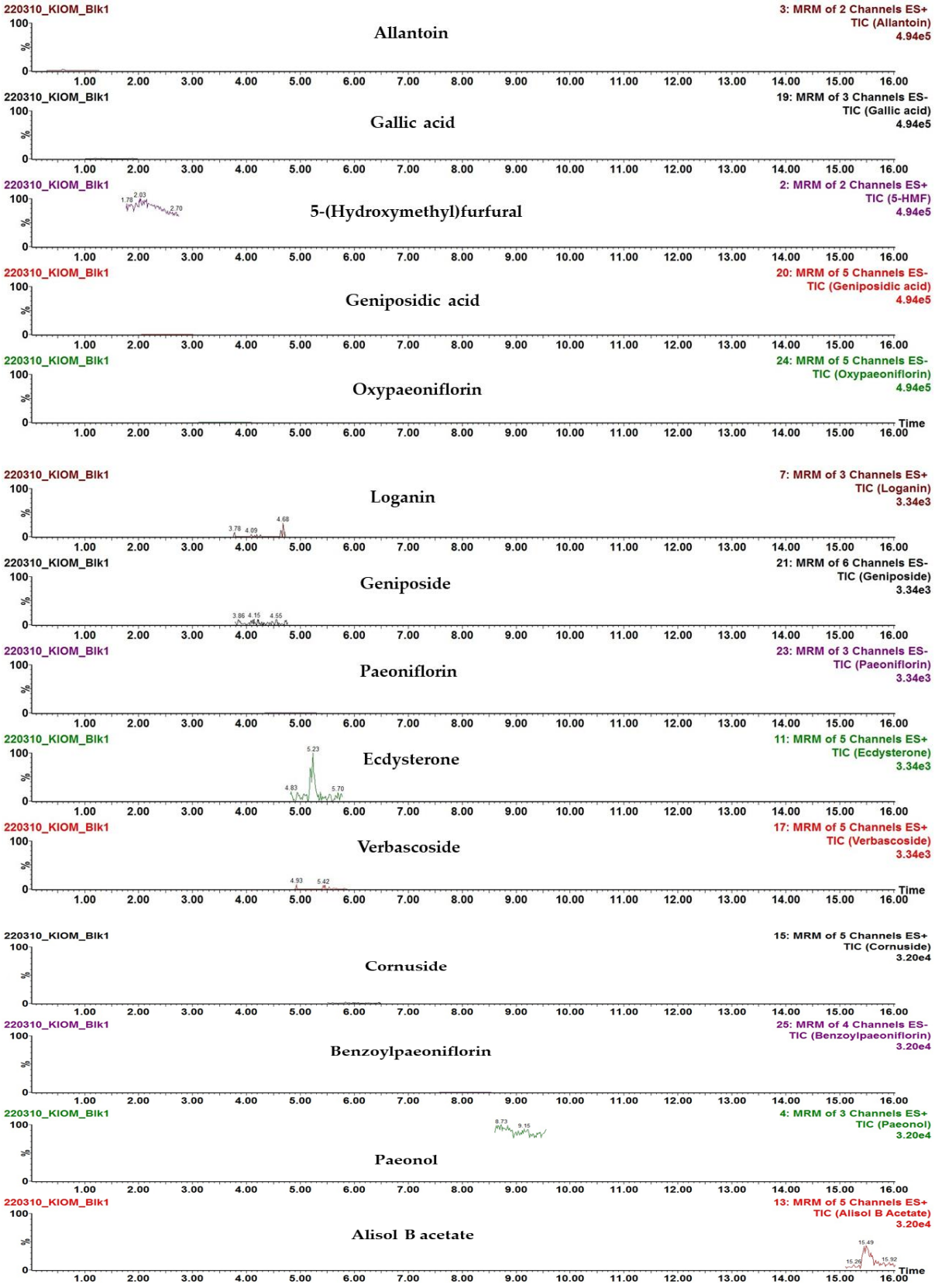
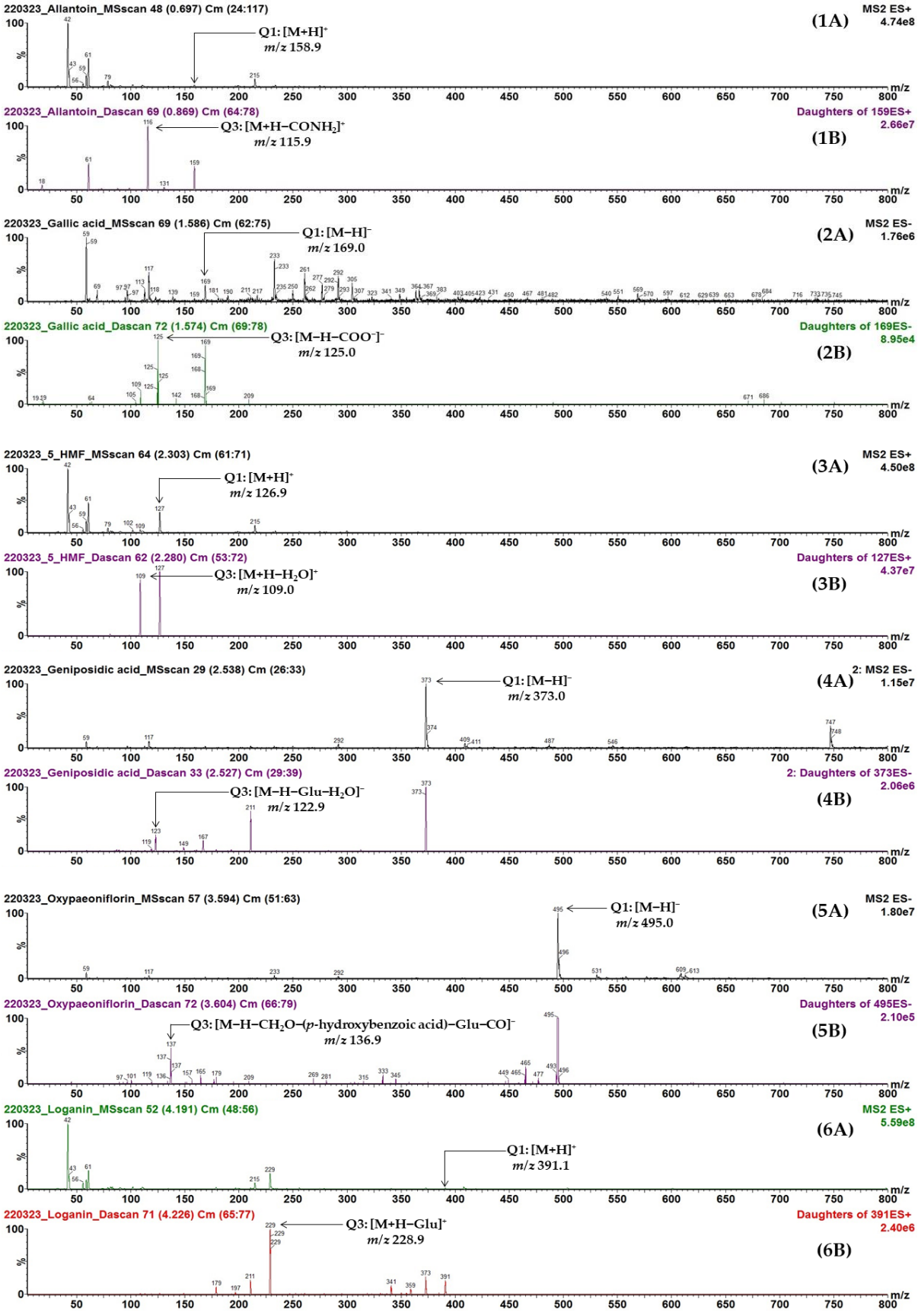
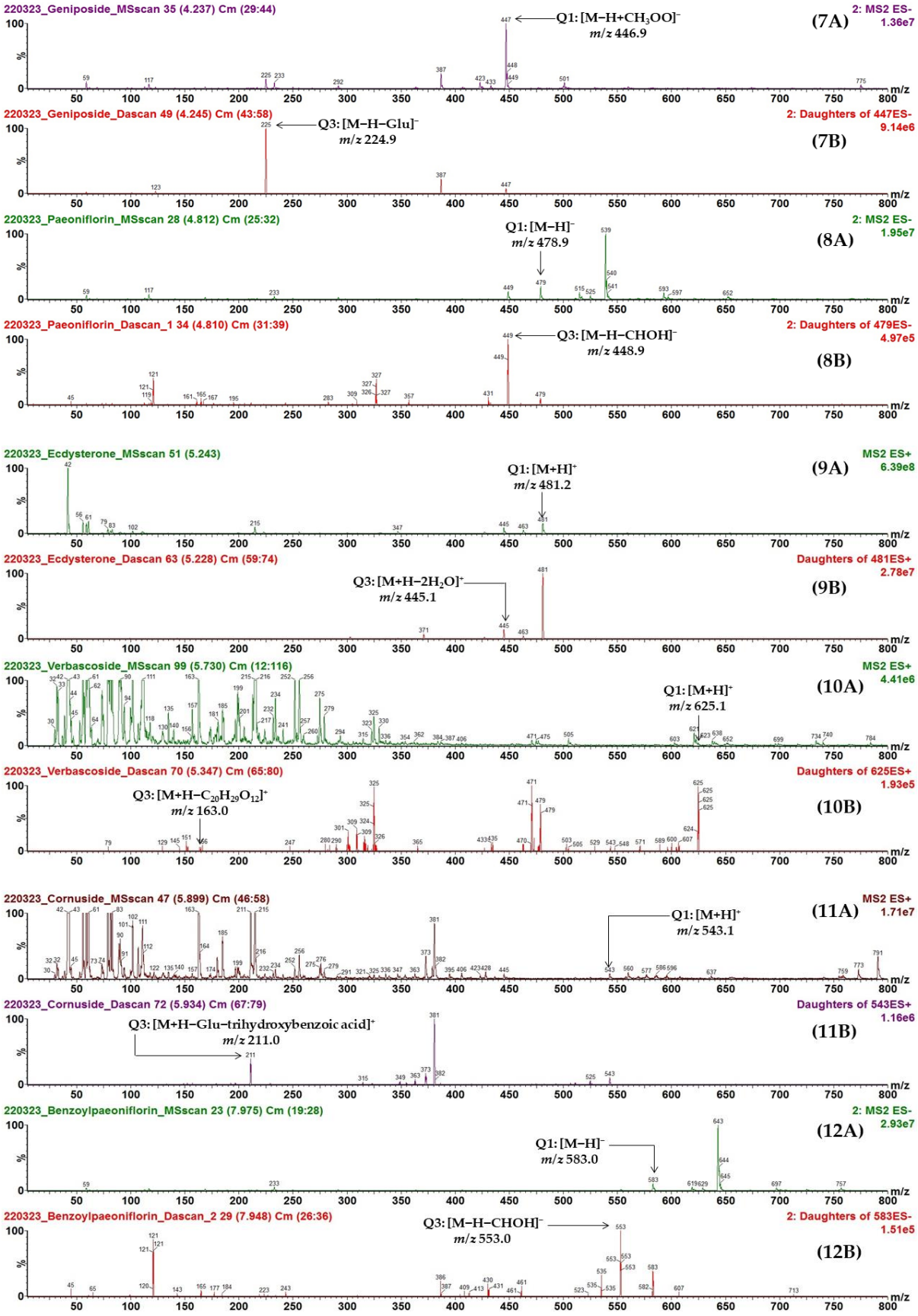


Figure S2. Extracted ion chromatograms for blank of each marker compound.


220323_Allantoin_MSscan 48 (0.697) Cm (24:117)
MS2 ES+
4.74e8
(1A)
Q1: [M+H]+
m/z 158.9
220323_Allantoin_Dascan 69 (0.869) Cm (64:78)
Daughters of 159ES+
2.66e7
(1B)
Q3: [M+H−CONH2]+
m/z 115.9
220323_Gallic acid_MSscan 69 (1.586) Cm (62:75)
MS2 ES-
1.76e6
(2A)
Q1: [M−H]−
m/z 169.0
220323_Gallic acid_Dascan 72 (1.574) Cm (69:78)
Daughters of 169ES-
8.95e4
(2B)
Q3: [M−H−COO−]−
m/z 125.0
220323_5_HMF_MSscan 64 (2.303) Cm (61:71)
MS2 ES+
4.50e8
(3A)
Q1: [M+H]+
m/z 126.9
220323_5_HMF_Dascan 62 (2.280) Cm (53:72)
Daughters of 127ES+
4.37e7
(3B)
Q3: [M+H−H2O]+
m/z 109.0
220323_Geniposidic acid_MSscan 29 (2.538) Cm (26:33)
2: MS2 ES-
1.15e7
(4A)
Q1: [M−H]−
m/z 373.0
220323_Geniposidic acid_Dascan 33 (2.527) Cm (29:39)
2: Daughters of 373ES-
2.06e6
(4B)
Q3: [M−H−Glu−H2O]−
m/z 122.9
220323_Oxypaeoniflorin_MSscan 57 (3.594) Cm (51:63)
MS2 ES-
1.80e7
(5A)
Q1: [M−H]−
m/z 495.0
220323_Oxypaeoniflorin_Dascan 72 (3.604) Cm (66:79)
Daughters of 495ES-
2.10e5
(5B)
Q3: [M−H−CH2O−(p-hydroxybenzoic acid)−Glu−CO]−
m/z 136.9
220323_Loganin_MSscan 52 (4.191) Cm (48:56)
MS2 ES+
5.59e8
(6A)
Q1: [M+H]+
m/z 391.1
220323_Loganin_Dascan 71 (4.226) Cm (65:77)
Daughters of 391ES+
2.40e6
(6B)
Q3: [M+H−Glu]+
m/z 228.9


220323_Geniposide_MSscan 35 (4.237) Cm (29:44)
Q1: [M−H+CH3OO]−
m/z 446.9
(7A)
2: MS2 ES-
1.36e7
220323_Geniposide_Dascan 49 (4.245) Cm (43:58)
Q3: [M−H−Glu]−
m/z 224.9
(7B)
2: Daughters of 447ES-
9.14e6
220323_Paeoniflorin_MSscan 28 (4.812) Cm (25:32)
Q1: [M−H]−
m/z 478.9
(8A)
2: MS2 ES-
1.95e7
220323_Paeoniflorin_Dascan_1 34 (4.810) Cm (31:39)
Q3: [M−H−CHOH]−
m/z 448.9
(8B)
2: Daughters of 479ES-
4.97e5
220323_Ecdysterone_MSscan 51 (5.243)
Q1: [M+H]+
m/z 481.2
(9A)
MS2 ES+
6.39e8
220323_Ecdysterone_Dascan 63 (5.228) Cm (59:74)
Q3: [M+H−2H2O]+
m/z 445.1
(9B)
Daughters of 481ES+
2.78e7
220323_Verbascoside_MSscan 99 (5.730) Cm (12:116)
Q1: [M+H]+
m/z 625.1
(10A)
MS2 ES+
4.41e6
220323_Verbascoside_Dascan 70 (5.347) Cm (65:80)
Q3: [M+H−C20H29O12]+
m/z 163.0
(10B)
Daughters of 625ES+
1.93e5
220323_Cornuside_MSscan 47 (5.899) Cm (46:58)
Q1: [M+H]+
m/z 543.1
(11A)
MS2 ES+
1.71e7
220323_Cornuside_Dascan 72 (5.934) Cm (67:79)
Q3: [M+H−Glu−trihydroxybenzoic acid]+
m/z 211.0
(11B)
Daughters of 543ES+
1.16e6
220323_Benzoylpaeoniflorin_MSscan 23 (7.975) Cm (19:28)
Q1: [M−H]−
m/z 583.0
(12A)
2: MS2 ES-
2.93e7
220323_Benzoylpaeoniflorin_Dascan_2 29 (7.948) Cm (26:36)
Q3: [M−H−CHOH]−
m/z 553.0
(12B)
2: Daughters of 583ES-
1.51e5
m/z

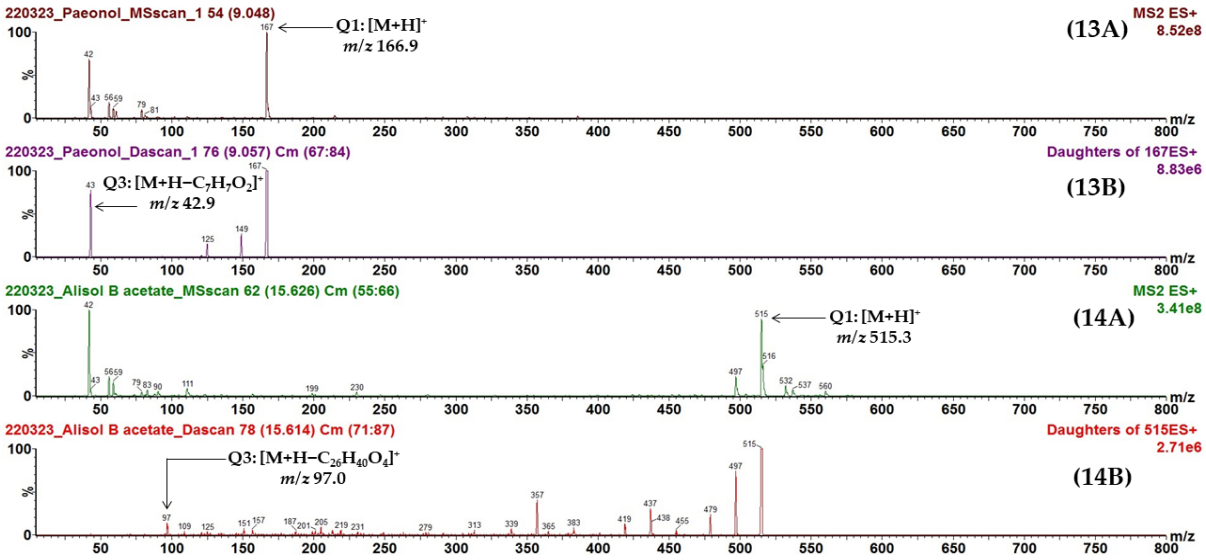
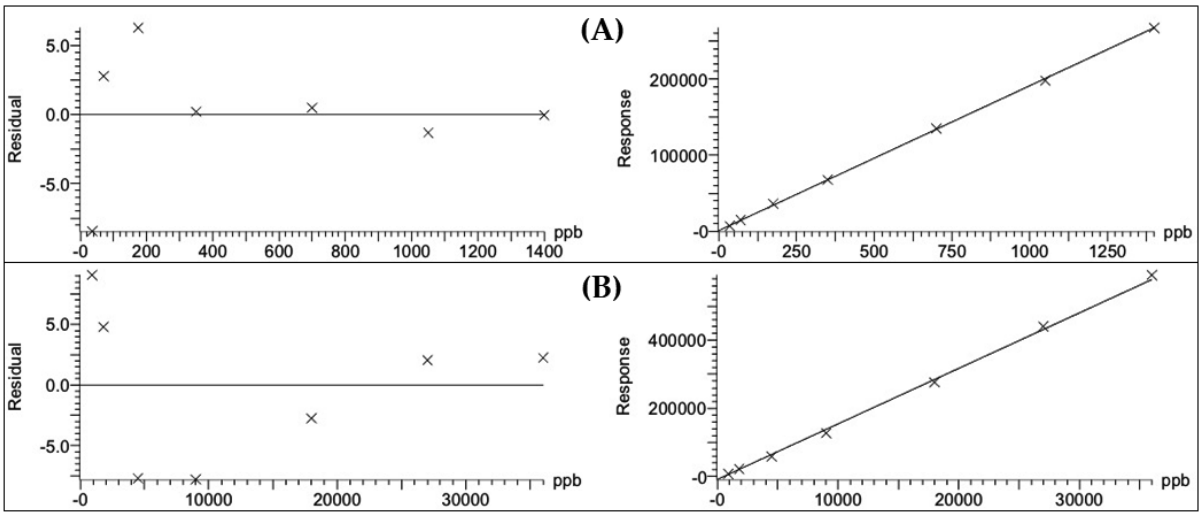
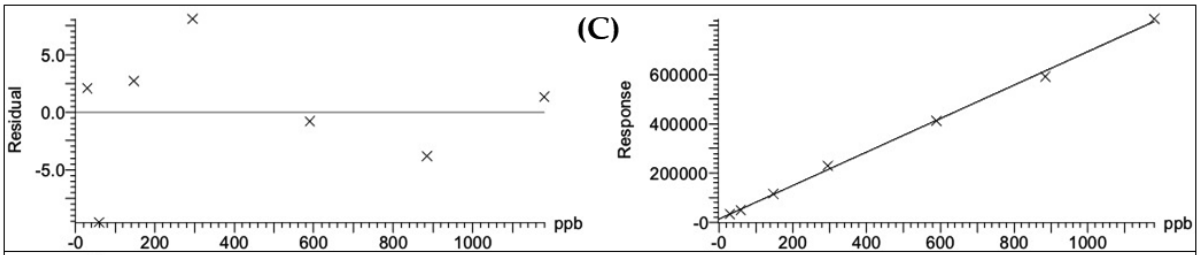
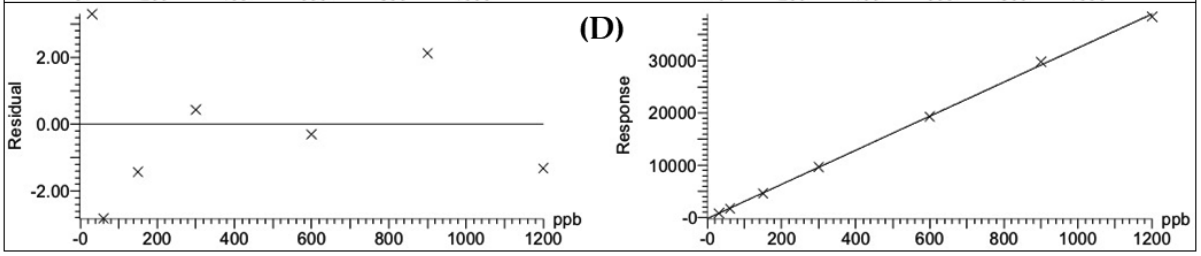


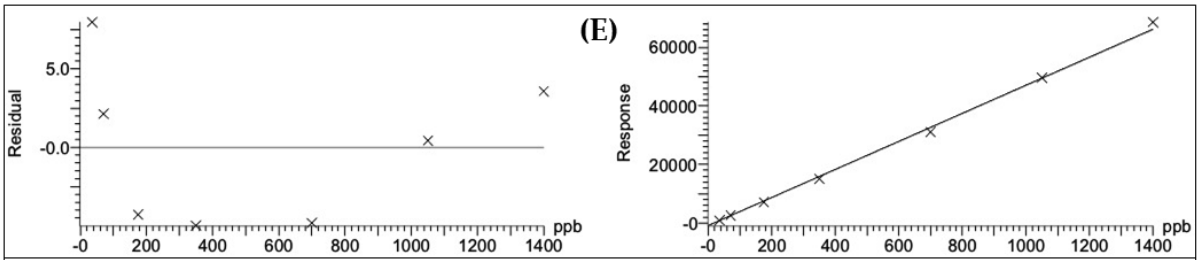
Figure S3. Q1 (A) and Q3 (B) mass spectra of 14 marker components. Allantoin (**1**), gallic acid (**2**), 5-(hydroxymethyl)furfural (**3**), geniposidic acid (**4**), oxypaeoniflorin (**5**), loganin (**6**), geniposide (**7**), paeoniflorin (**8**), ecdysterone (**9**), verbascoside (**10**), cornuside (**11**), benzoylpaeoniflorin (**12**), paeonol (**13**), and alisol B acetate (**14**).

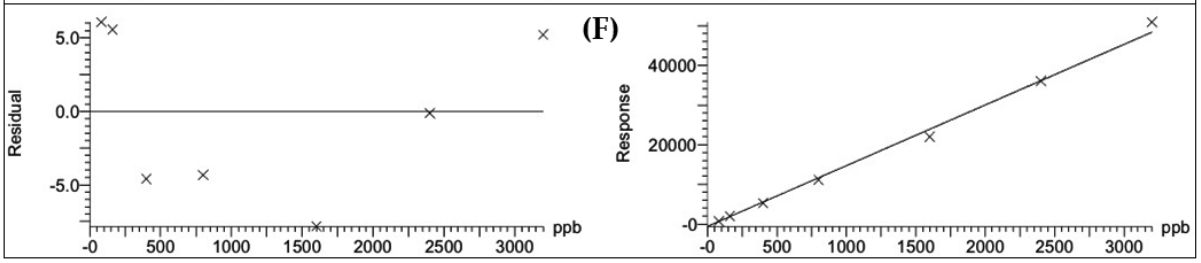

(A)
Residual
5.0
0.0
-5.0
-0
200
400
600
800
1000
1200
1400
ppb
Response
200000
100000
-0
250
500
750
1000
1250
ppb

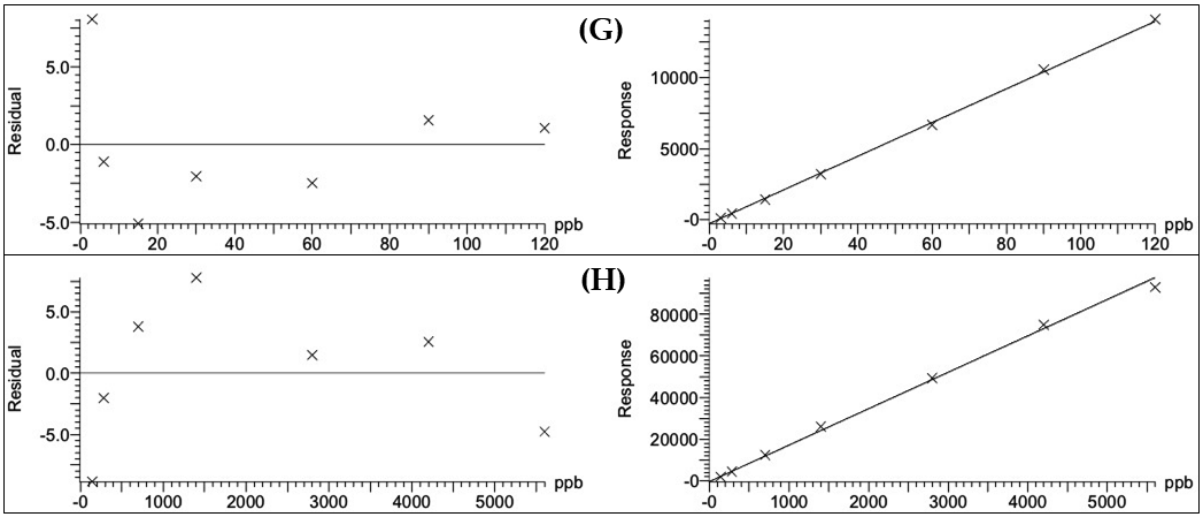
(B)
Residual
5.0
0.0
-5.0
-0
10000
20000
30000
ppb
Response
400000
200000
-0
10000
20000
30000
ppb


(C)
Residual
5.0
0.0
-5.0
-0
200
400
600
800
1000
ppb
Response
600000
400000
200000
-0
200
400
600
800
1000
ppb

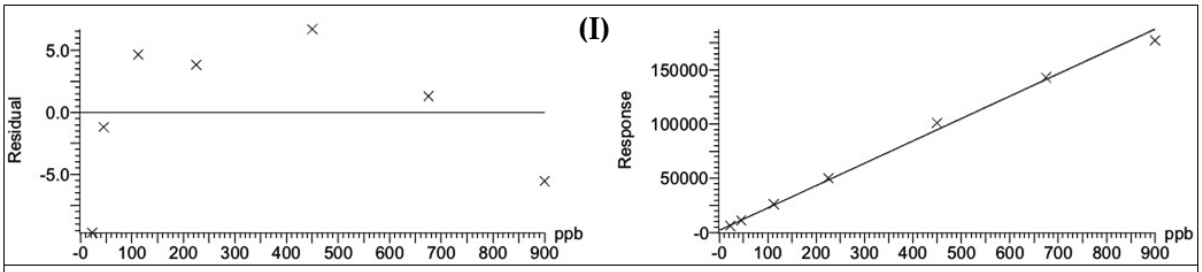

(D)
Residual
2.00
0.00
-2.00
-0
200
400
600
800
1000
1200
ppb
Response
30000
20000
10000
-0
200
400
600
800
1000
1200
ppb

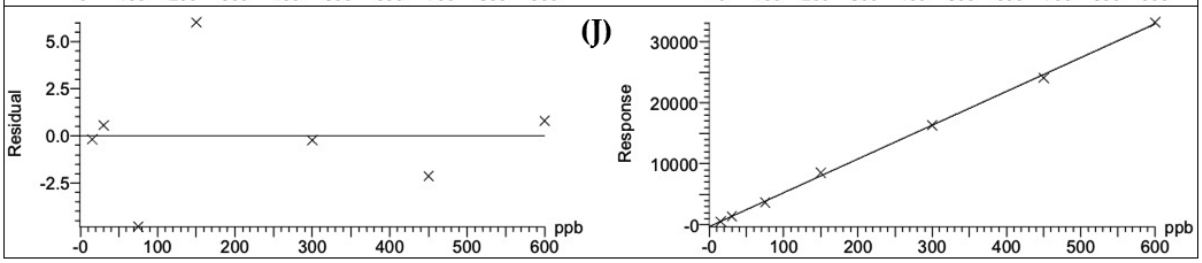

(E)
Residual
5.0
-0.0
-0
200
400
600
800
1000
1200
1400
ppb
Response
60000
40000
20000
-0
200
400
600
800
1000
1200
1400
ppb

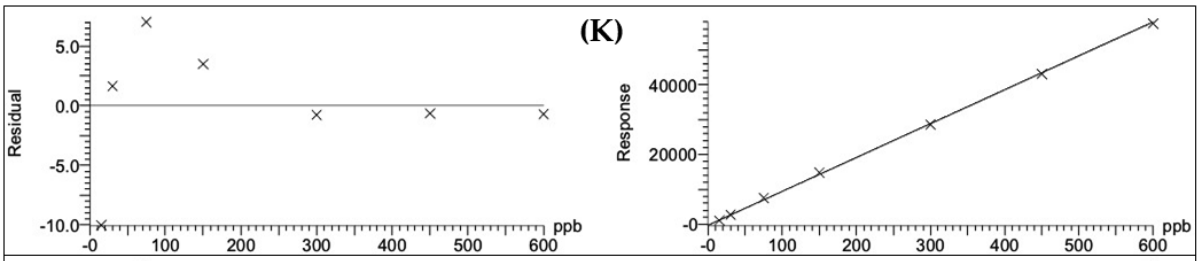

(F)
Residual
5.0
0.0
-5.0
-0
500
1000
1500
2000
2500
3000
ppb
Response
40000
20000
-0
500
1000
1500
2000
2500
3000
ppb

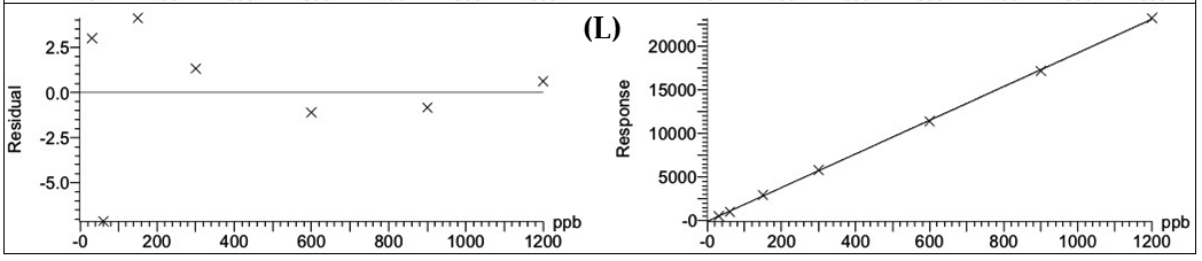

(G)
Residual
5.0
0.0
-5.0
-0 20 40 60 80 100 120
ppb
Response
10000
5000
-0 20 40 60 80 100 120
ppb

(H)
Residual
5.0
0.0
-5.0
-0 1000 2000 3000 4000 5000
ppb
Response
80000
60000
40000
20000
-0 1000 2000 3000 4000 5000
ppb


(I)
Residual
5.0
0.0
-5.0
-0 100 200 300 400 500 600 700 800 900
ppb
Response
150000
100000
50000
-0 100 200 300 400 500 600 700 800 900
ppb


(J)
Residual
5.0
2.5
0.0
-2.5
-0 100 200 300 400 500 600
ppb
Response
30000
20000
10000
-0 100 200 300 400 500 600
ppb


(K)
Residual
5.0
0.0
-5.0
-10.0
-0 100 200 300 400 500 600
ppb
Response
40000
20000
-0 100 200 300 400 500 600
ppb


(L)
Residual
2.5
0.0
-2.5
-5.0
-0 200 400 600 800 1000 1200
ppb
Response
20000
15000
10000
5000
-0 200 400 600 800 1000 1200
ppb

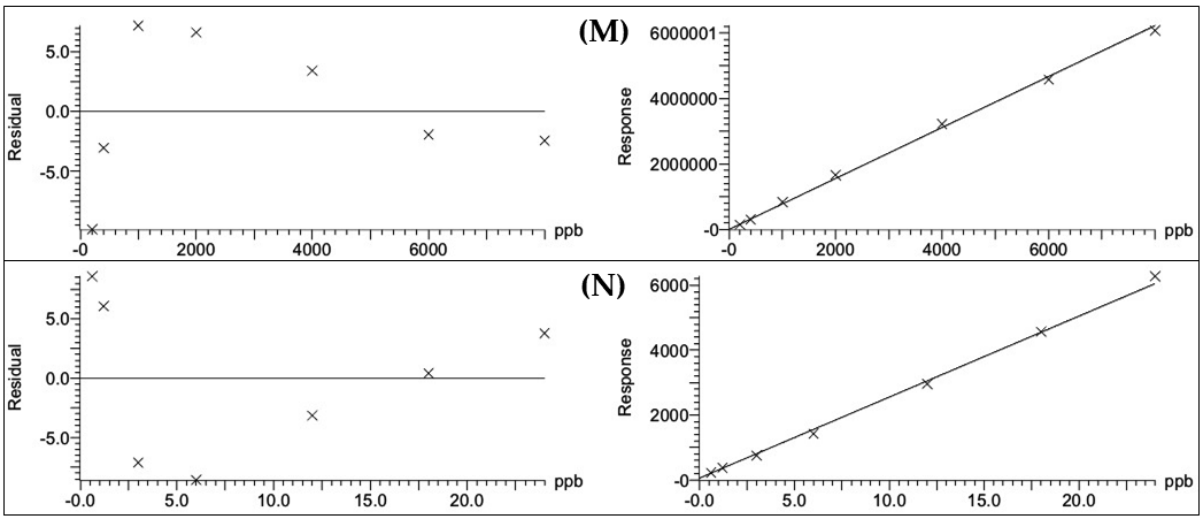


Figure S4. Calibration curves and residuals of 14 marker components. A; allantoin, B; gallic acid, C; 5-(hydroxymethyl)furfural, D; geniposidic acid, E; oxypaeoniflorin, F; loganin, G; geniposide, H; paeoniflorin, I; ecdysterone, J; verbascoside, K; cornuside, L; benzoylpaeoniflorin, M; paeonol, and N; alisol B acetate.

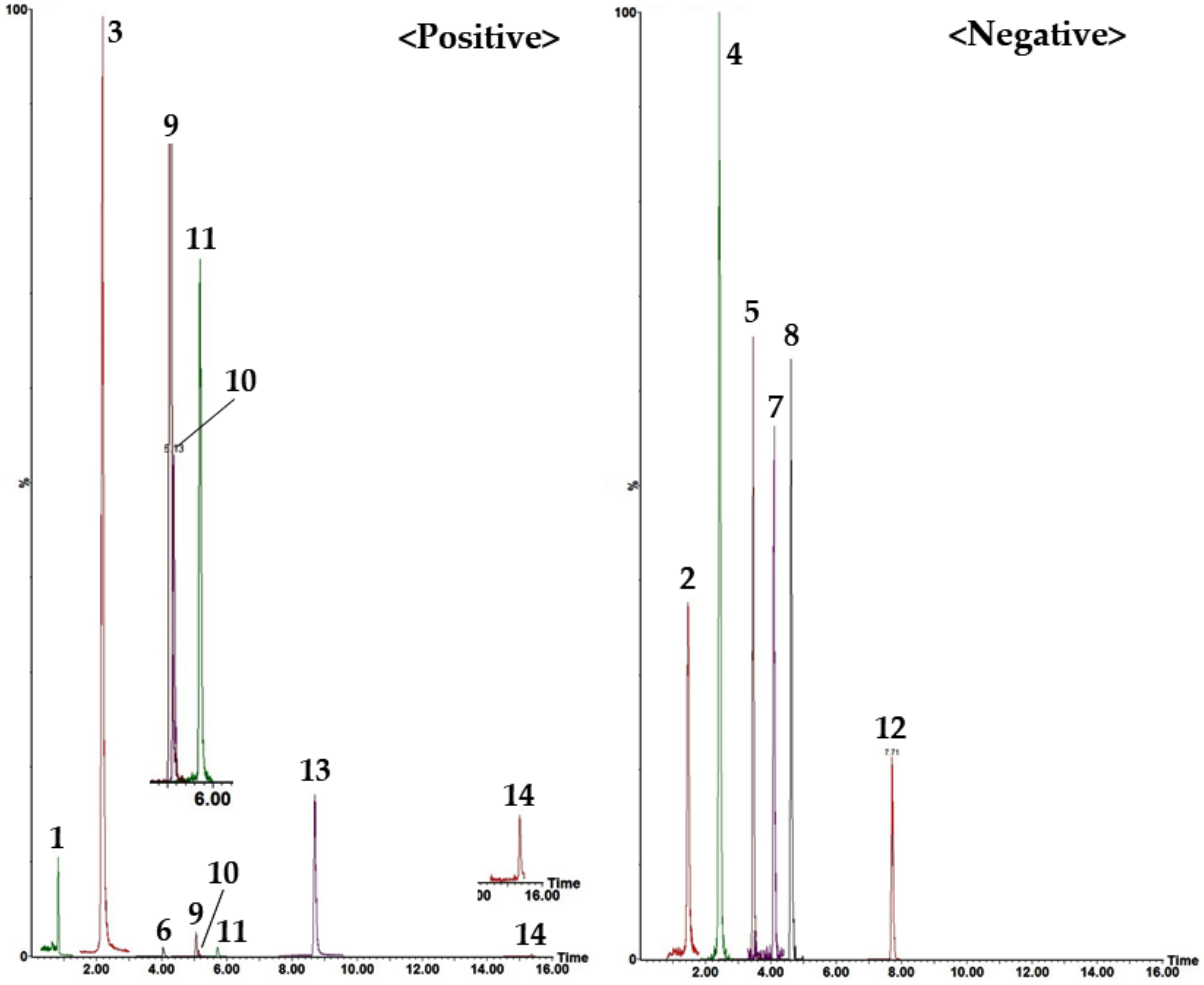
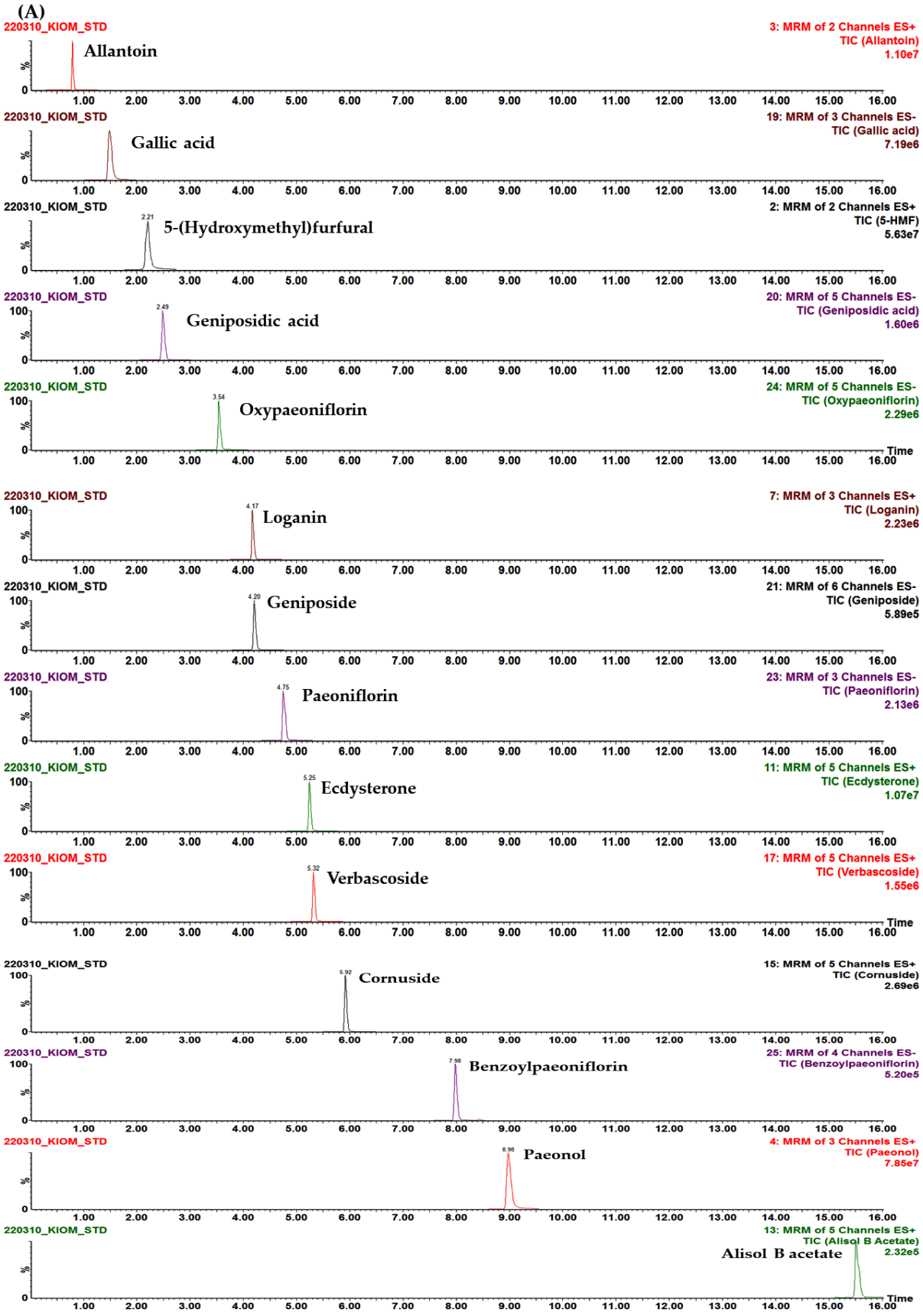


Figure S5. Total ion chromatogram of LOD using the UPLC–MS/MS MRM method in the positive and negative ion modes.


(A)
220310_KIOM_STD
3: MRM of 2 Channels ES+
TIC (Allantoin)
1.10e7
Allantoin
220310_KIOM_STD
19: MRM of 3 Channels ES-
TIC (Gallic acid)
7.19e6
Gallic acid
220310_KIOM_STD
2: MRM of 2 Channels ES+
TIC (5-HMF)
5.63e7
2.21
5-(Hydroxymethyl)furfural
220310_KIOM_STD
20: MRM of 5 Channels ES-
TIC (Geniposidic acid)
1.60e6
2.49
Geniposidic acid
220310_KIOM_STD
24: MRM of 5 Channels ES-
TIC (Oxypaeoniflorin)
2.29e6
3.54
Oxypaeoniflorin
220310_KIOM_STD
7: MRM of 3 Channels ES+
TIC (Loganin)
2.23e6
4.17
Loganin
220310_KIOM_STD
21: MRM of 6 Channels ES-
TIC (Geniposide)
5.89e5
4.20
Geniposide
220310_KIOM_STD
23: MRM of 3 Channels ES-
TIC (Paeoniflorin)
2.13e6
4.75
Paeoniflorin
220310_KIOM_STD
11: MRM of 5 Channels ES+
TIC (Ecdysterone)
1.07e7
5.25
Ecdysterone
220310_KIOM_STD
17: MRM of 5 Channels ES+
TIC (Verbascoside)
1.55e6
5.32
Verbascoside
220310_KIOM_STD
15: MRM of 5 Channels ES+
TIC (Cornuside)
2.69e6
5.92
Cornuside
220310_KIOM_STD
25: MRM of 4 Channels ES-
TIC (Benzoylpaeoniflorin)
5.20e5
7.98
Benzoylpaeoniflorin
220310_KIOM_STD
4: MRM of 3 Channels ES+
TIC (Paeonol)
7.85e7
8.98
Paeonol
220310_KIOM_STD
13: MRM of 5 Channels ES+
TIC (Alisol B Acetate)
2.32e5
Alisol B acetate
%
Time
1.00 2.00 3.00 4.00 5.00 6.00 7.00 8.00 9.00 10.00 11.00 12.00 13.00 14.00 15.00 16.00

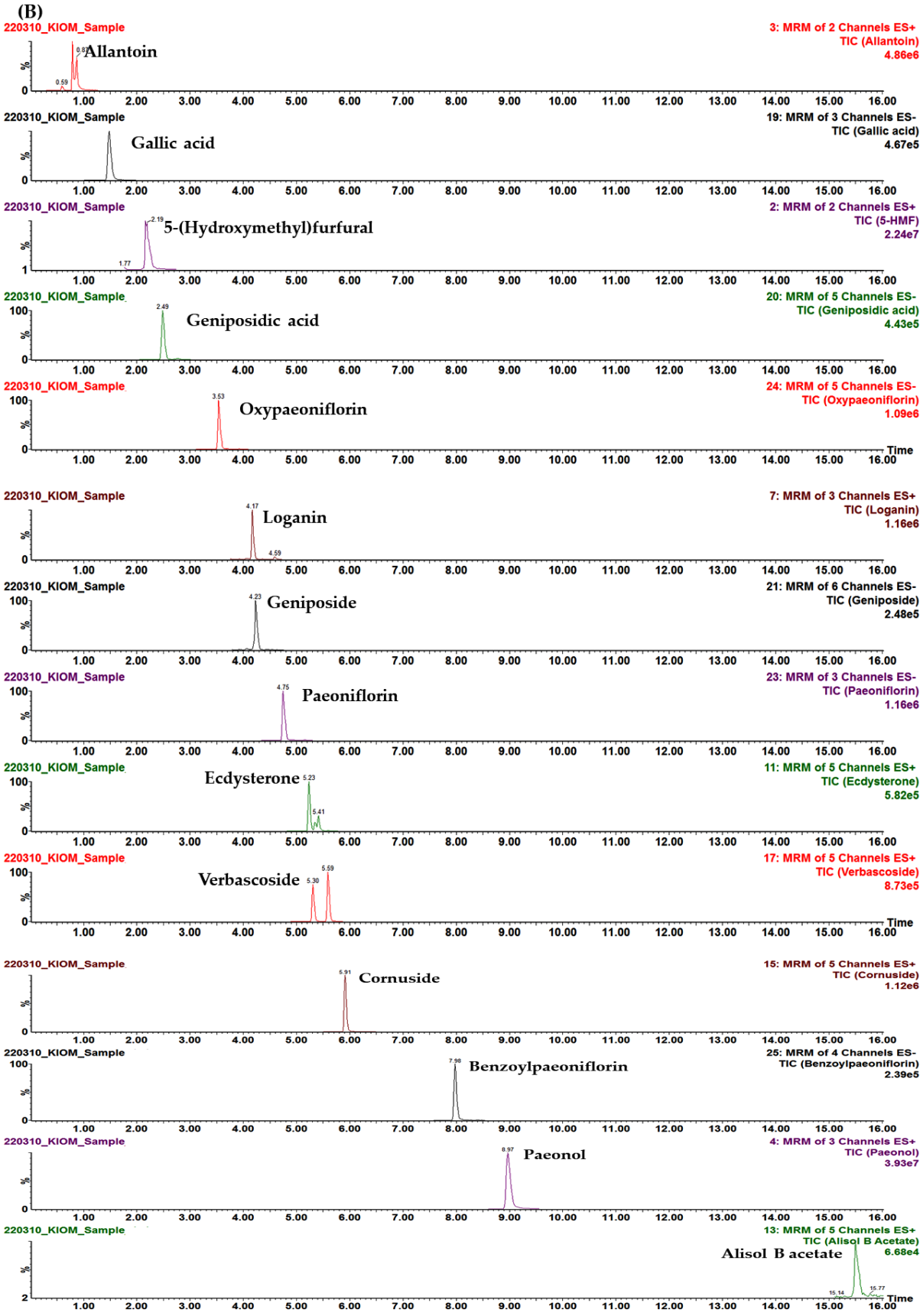
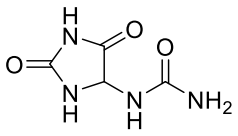
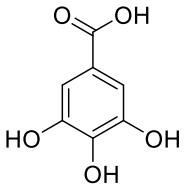

(B)
220310_KIOM_Sample
3: MRM of 2 Channels ES+
TIC (Allantoin)
4.86e6
Allantoin
0.88
0.59
220310_KIOM_Sample
19: MRM of 3 Channels ES-
TIC (Gallic acid)
4.67e5
Gallic acid
220310_KIOM_Sample
2: MRM of 2 Channels ES+
TIC (5-HMF)
2.24e7
5-(Hydroxymethyl)furfural
2.19
1.77
220310_KIOM_Sample
20: MRM of 5 Channels ES-
TIC (Geniposidic acid)
4.43e5
Geniposidic acid
2.49
220310_KIOM_Sample
24: MRM of 5 Channels ES-
TIC (Oxypaeoniflorin)
1.09e6
Oxypaeoniflorin
3.53
Time
220310_KIOM_Sample
7: MRM of 3 Channels ES+
TIC (Loganin)
1.16e6
Loganin
4.17
4.59
220310_KIOM_Sample
21: MRM of 6 Channels ES-
TIC (Geniposide)
2.48e5
Geniposide
4.23
220310_KIOM_Sample
23: MRM of 3 Channels ES-
TIC (Paeoniflorin)
1.16e6
Paeoniflorin
4.75
220310_KIOM_Sample
11: MRM of 5 Channels ES+
TIC (Ecdysterone)
5.82e5
Ecdysterone
5.23
5.41
220310_KIOM_Sample
17: MRM of 5 Channels ES+
TIC (Verbascoside)
8.73e5
Verbascoside
5.30
5.59
Time
220310_KIOM_Sample
15: MRM of 5 Channels ES+
TIC (Cornuside)
1.12e6
Cornuside
5.91
220310_KIOM_Sample
25: MRM of 4 Channels ES-
TIC (Benzoylpaeoniflorin)
2.39e5
Benzoylpaeoniflorin
7.98
220310_KIOM_Sample
4: MRM of 3 Channels ES+
TIC (Paeonol)
3.93e7
Paeonol
8.97
220310_KIOM_Sample
13: MRM of 5 Channels ES+
TIC (Alisol B Acetate)
6.68e4
Alisol B acetate
15.14
15.77
Time

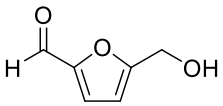
Figure S6. Extracted ion chromatograms of each marker compound (A) and GSH sample (B) using the UPLC–MS/MS MRM method in the positive and negative ion modes.



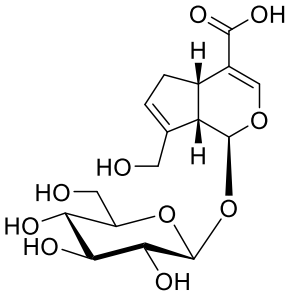
Allantoin (**1**)



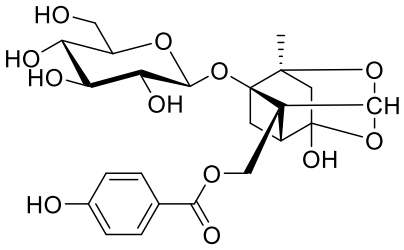
Gallic acid (**2**)



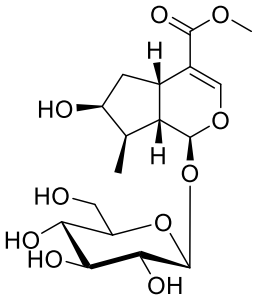
5-(Hydroxymethyl)furfural (**3**)



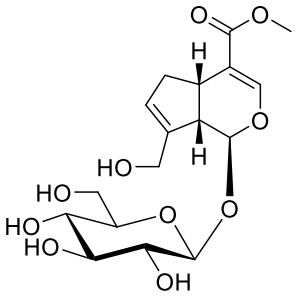
Geniposidic acid (**4**)



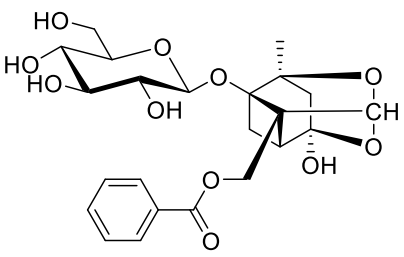
Oxypaeoniflorin (**5**)



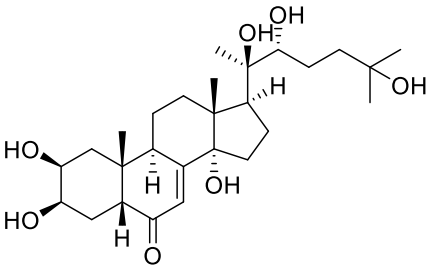
Loganin (**6**)



Geniposide (**7**)



Paeoniflorin (**8**)



Ecdysterone (**9**)

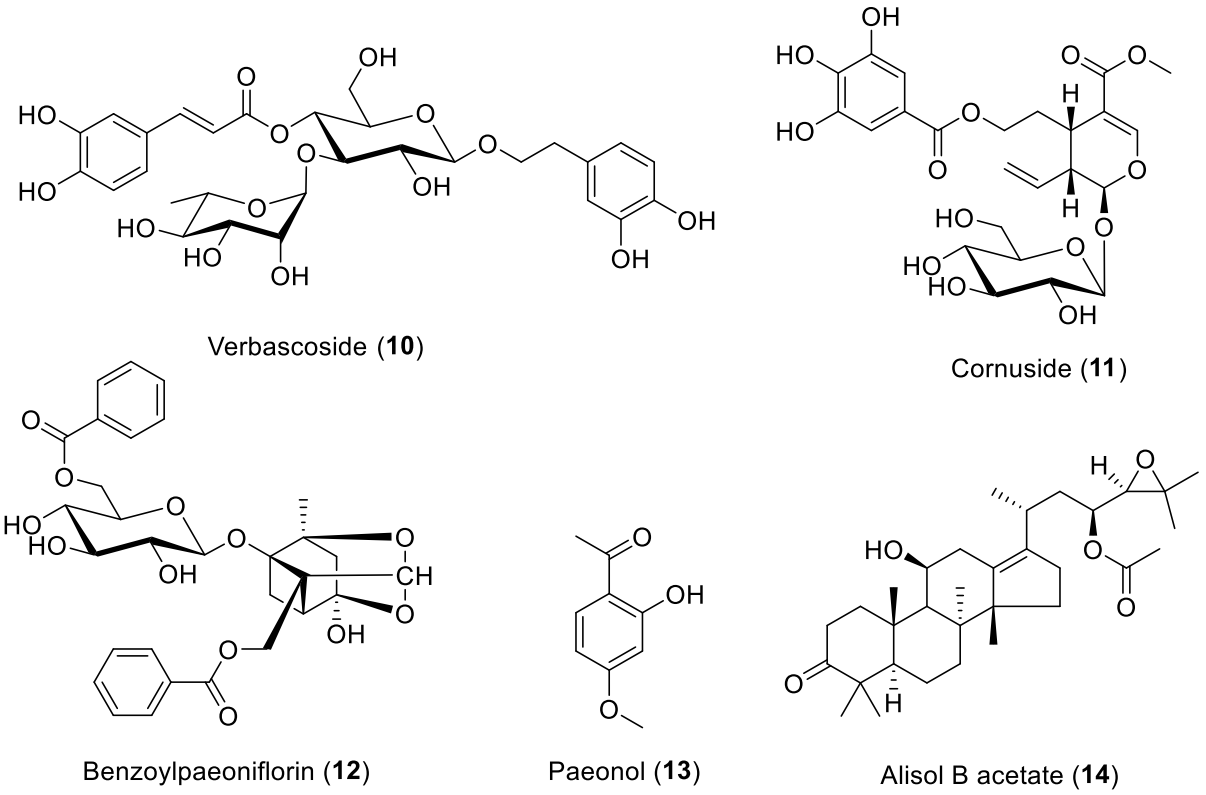


Figure S7. Chemical structures of the 14 marker components in GSH.