

Supplementary material

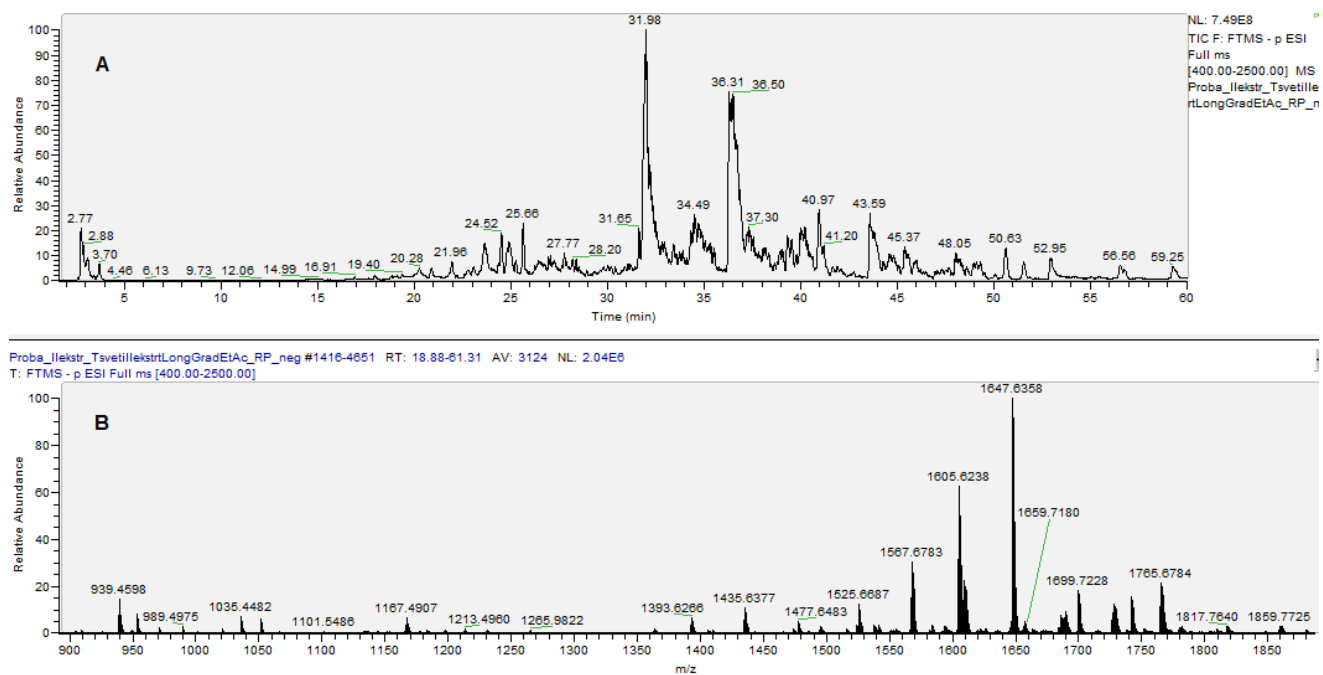
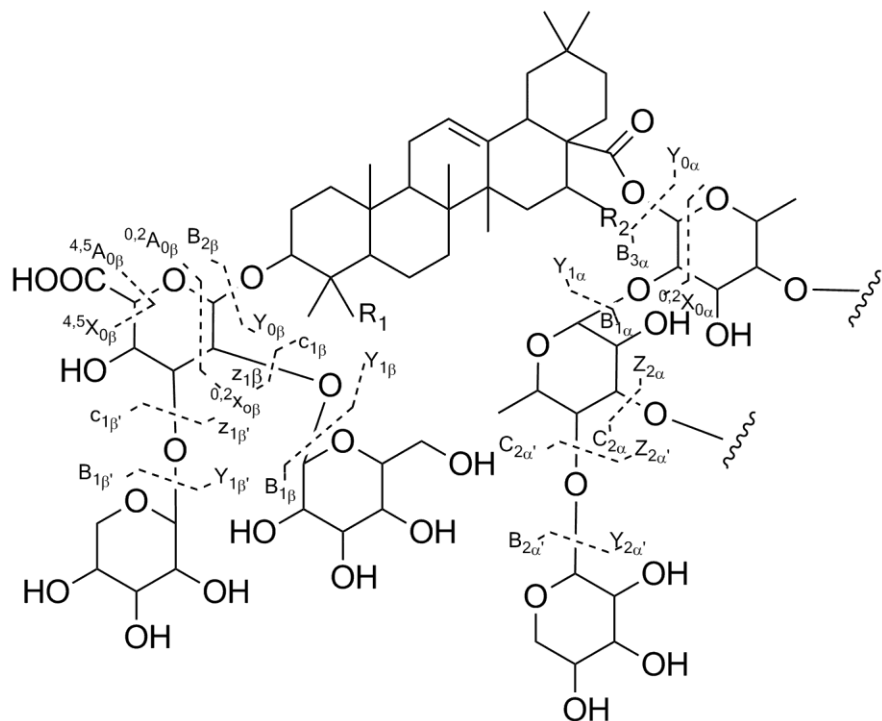


Fig. S1. Total ion chromatogram (TIC) of *G. trichotoma* root extract analyzed by UHPLC-HRMS in negative ion mode (A). ESI-MS spectra in the mass range 900.00-1900.00 m/z (according to the expected GOTCAB molecular masses) of the *G. trichotoma* root extract (B).

Table S1. Tentative assignment of GOTCAB saponins from *G. trichotoma* roots by MS and MS/MS data. Gypsogenin (G) R1= CHO, R2= H; Quillaic acid (QA) R1=CHO, R2=OH; Gypsogenic acid (GA) R1= COOH, R2= H; Oleanolic acid (OA) R1= CH₃, R2= H.



	Number of the separated isobaric isomers	t _R ^a min	Precursor ion [M-H] ⁻ (m/z)		Error ppm	Fragmentation pattern in MS/MS	Sapogenin	Tentative assignment	
			Exact mass Formula	Accurate mass				β chain	α chain
Monodesmosides									
1	2	24.91 25.64	1035.4476 C ₄₈ H ₇₅ O ₂₂ S	1035.4484 1035.4440*	0.717 -3.523	549.2864 (9.9) ^b , 505.2999 (100)	G ^c	SO ₃ H	3Hex
2	2	23.66 24.52	1051.44425 C ₄₈ H ₇₅ O ₂₃ S	1051.4418 1051.4436*	-0.725 1.016	1051.4436 (5.7), 565.1075 (30.7), 485.3270 (100),	GA	SO ₃ H	3Hex

						467.3175 (1.8), 439.3212 (2.5), 423.3265 (2.3)			
3	2	24.91 25.64	1167.4899 C ₅₃ H ₈₃ O ₂₆ S	1167.4933 1167.4901*	2.924 0.200	1167.4901 (16.9), 1035.4419 (0.5), 549.2888 (100), 519.2418 (4.4), 475.2540 (0.5)	G	SO ₃ H	3Hex, Pent
4	3	23.06 24.44 25.26	1197.5004 C ₅₄ H ₈₅ O ₂₇ S	1197.5005 1197.5005 1197.4999*	0.041 0.041 -0.010	1197.4999 (18.2), 1035.4484 (1.2), 549.2891 (100), 519.2421 (4.3), 505.3056 (0.2), 469.3319 (0.9)	G	SO ₃ H	4Hex
5	3	20.28 21.94 22.79	1213.4954 C ₅₄ H ₈₅ O ₂₈ S	1213.4952 1213.4951 1213.4956*	-0.095 -0.194 0.210	1213.4956 (1.0), 727.1618 (20.1), 565.1071 (2.6), 485.3271 (100), 467.3157 (3.4), 423.3274 (4.1)	GA	SO ₃ H	4Hex
6	1	40.94	939.4595 C ₄₇ H ₇₁ O ₁₉	939.4600	0.529	583.3647 (5.4), 565.3479 (5.1), 551.3372 (8.7), 469.3333 (43.5), 451.3223 (16.8)	G	Pent, Hex, HexA	-
Bidesmosides with C-28 oligosaccharide (type I)									
7	2	33.87 34.01	1363.6176 C ₆₄ H ₉₉ O ₃₁	1363.6162 1363.6166*	-1.001 -0.733	1231.5666 (5.9), 939.4621 (28.8), 583.3636 (21.4), 565.3535 (8.1), 551.3391 (11.7), 469.3322 (100), 451.3208 (11.0), 423.3267 (6.3)	G	Pent, Hex, HexA ^d	2dHex, Pent
8	2	32.85 32.97	1393.6281 C ₆₅ H ₁₀₁ O ₃₂	1393.6296 1393.6276*	1.079 -0.419	1393.6276 (62.4) [M-H] ⁻ 1261.5653 (0.6) [M-H-Pent] ⁻ 939.4605 (100) [M-H- α chain] ⁻ (Y _{0α}) ^d 807.4171 (7.8) [Y _{0α} -H-Pent] ⁻ 789.4051 (0.8) [M-H- α chain- Pent-H ₂ O] ⁻ = Y _{0α} /Z _{1β} 759.3972 (10.5) [M-H- α chain- Hex-H ₂ O] ⁻ = Y _{0α} /Z _{1β} 745.4167 (5.8) [M-H- α chain- Pent-H ₂ O-CO ₂] ⁻ = Y _{0α} /Z _{1β} /CO ₂ 727.4092 (1.6) [M-H- α chain- Pent-2H ₂ O-CO ₂] ⁻ = Y _{0α} /Z _{1β} /H ₂ O/CO ₂ 697.3962 (0.9) [M-H- α chain- Hex-2H ₂ O-CO ₂] ⁻ = Y _{0α} /Z _{1β} /H ₂ O/CO ₂ 627.3530 (2.3) [M-H- α chain-	G	Pent, Hex, HexA ^d	2dHex, Hex

					<p> Pent-Hex-H₂O]⁻ = Y_{0α}/Z_{1β}/Y_{1β} или Y_{0α}/Z_{1β}/Y_{1β} 609.3417 (2.6) [M-H-α chain- Pent-Hex-2H₂O]⁻ = Y_{0α}/Z_{1β}/Z_{1β} 583.3635 (6.5) [M-H-α chain- Pent-Hex-H₂O-CO₂]⁻ = Y_{0α}/Z_{1β}/Y_{1β}/CO₂ 565.3528 (13.6) [M-H-α chain- Pent-Hex-2H₂O-CO₂]⁻ = Y_{0α}/Z_{1β}/Z_{1β}/CO₂ 551.3374 (8.2) [M-H-α chain- Pent-Hex-2H₂O-58]⁻ = Y_{0α}/Z_{1β}/Z_{1β}^{4,5}A_{0β} 547.3409 (2.4) [M-H-α chain- Pent-Hex-3H₂O-CO₂]⁻ = Y_{0α}/Z_{1β}/Z_{1β}/H₂O/CO₂ 537.3573 (3.7) [M-H-α chain- Pent-Hex-H₂O-HCO₂H-CO₂]⁻ = Y_{0α}/Y_{1β}/Y_{1β}'/H₂O/HCO₂H/ CO₂ 519.3444 (0.8) [M-H-α chain- Pent-Hex-2H₂O-HCO₂H-CO₂]⁻ = Y_{0α}/Z_{1β}/Z_{1β}/HCO₂H/CO₂ 495.3470 (0.7) Y_{0α}^{0,2}X_{0β}/Z_{1β}/Z_{1β} 469.3322 (32.2) [gypsogenin-H]⁻ 451.3213 (4.2) [gypsogenin-H- H₂O]⁻ 439.3192 (0.6) [gypsogenin-H- H₂CO]⁻ 423.3237 (1.6) [gypsogenin-H- HCO₂H]⁻ 319.0662 (0.4) [β chain-H-Pent- H₂O] = B_{2β}/Z_{1β} 301.0554 (0.6) [β chain-H-Pent- 2H₂O] = B_{2β}/Z_{1β}/H₂O 289.0540 (0.2) [β chain-H-Hex- H₂O] = B_{2β}/Z_{1β} 271.0457 (0.3) [β chain-H-Hex- 2H₂O] = B_{2β}/Z_{1β}/H₂O 157.0107 (2.1) [β chain-H-Pent- </p>		
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						Hex- H ₂ O] = B _{2β} /Z _{1β} /Y _{1β} ⁺ 139.0002 (2.1) [β chain-H-Pent- Hex-2H ₂ O] = B _{2β} /Z _{1β} /Z _{1β} ⁺ 131.0319 (0.5) [Pent-H] ⁻			
9		33.11	1481.6806 C ₆₉ H ₁₀₉ O ₃₄	1481.6802	-0.265	1481.6802 (91.5), 925.4805 (100), 551.3737 (37.6), 455.3528 (65.7), 437.3441 (10.2), 423.1463 (0.6), 407.3300 (1.0)	OA	Pent, Hex, HexA ^d	2dHex, 2Pent
10	2	33.24 33.39	1495.6598 C ₆₉ H ₁₀₇ O ₃₅	1495.6620* 1495.6589	1.439 -0.600	1495.6620 (13.3), 939.4619 (100), 469.3329 (38.2)	G	Pent, Hex, HexA ^d	2dHex, 2Pent
11	2	30.74	1511.6548 C ₆₉ H ₁₀₇ O ₃₆	1511.6542	-0.385	1511.6542 (100), 955.4550 (91.1), 775.3934 (10.5), 485.3271 (18.5), 405.3180 (16.1)	QA	Pent, Hex, HexA ^d	2dHex, 2Pent
12	1	30.98	1511.6548 C ₆₉ H ₁₀₇ O ₃₆	1511.6572	1.619	1511.6572 (83.4), 939.4601 (86.8), 565.3526 (31.4), 469.3319 (100), 423.3261 (10.3)	G	Pent, Hex, HexA ^d	dHex, 2Pent, Hex
13	2	32.49 32.69	1525.6704 C ₇₀ H ₁₀₉ O ₃₆	1525.6705 1525.6714*	0.084 0.647	1525.6714 (40.1), 939.4606 (100), 469.3320 (42.1), 423.3270 (2.8)	G	Pent, Hex, HexA ^d	2dHex, Pent, Hex
14	2	30.22 30.40	1541.6653 C ₇₀ H ₁₀₉ O ₃₇	1541.6646* 1541.6642	-0.497 -0.737	955.4474 (100), 823.4107 (15.1), 775.3893 (26.1), 761.4070 (15.3), 713.3921 (12.9), 581.3431 (25.4), 567.3318 (13.9), 485.3288 (51.0), 405.3162 (64.2)	QA	Pent, Hex, HexA ^d	2dHex, Pent, Hex
15	2	29.40 29.57	1805.7498 C ₈₀ H ₁₂₅ O ₄₅	1805.7487 1805.7477*	-0.650 -1.193	955.4581 (100), 775.3911 (15.6), 485.3271 (62.8), 405.3167 (99.9)	QA	Pent, Hex, HexA ^d	2dHex, 3Pent, Hex
Bidesmosides with C-28 oligosaccharide substituted with a sulfate group (type II)									
16	2	31.96 33.54	1443.5744 C ₆₄ H ₉₉ O ₃₄ S	1443.5739* 1443.5740	-0.376 -0.293	665.1601 (100), 607.1202 (6.0), 579.1238 (13.4), 519.1020 (24.1), 503.1081 (18.9), 371.0676 (6.0), 329.0180 (1.7), 259.0118 (10.4), 241.0015 (28.3)	G	Pent, HexA	2dHex, Pent, Hex, SO ₃ H
17	2	31.98 32.21	1605.6272 C ₇₀ H ₁₀₉ O ₃₉ S	1605.6292* 1605.6277	1.204 0.295	1605.6292 (32.2), 1525.6711 (2.1), 1135.5018 (11.2), 939.4608 (1.9), 665.1605 (100),	G	Pent, Hex, HexA ^d	2dHex, Pent, Hex, SO ₃ H

						469.3322 (1.0), 241.0018 (3.7)			
Bidesmosides with C-28 oligosaccharide substituted with acetyl group(s) (type III)									
18	2	35.05* 37.86	1435.6387 C ₆₇ H ₁₀₃ O ₃₃	1435.6404* 1435.6404		1435.6404 (54.5), 939.4604 (100), 469.3319 (42.0), 423.3266 (2.8)	G	Pent, Hex, HexA ^d	2dHex, Hex, Ac
19	2	40.41 40.57	1477.6493 C ₆₉ H ₁₀₅ O ₃₄	1477.6482 1477.6499*	-0.733 0.424	1477.6499 (100), 1435.6434 (0.9), 1345.6143 (1.3), 939.4612 (30.3), 745.4158 (6.7), 583.3654 (5.1), 565.3527 (15.3), 551.3373 (6.7), 469.3320 (27.4), 451.3203 (2.8), 423.3272 (1.8)	G	Pent, Hex, HexA ^d	2dHex, Hex, 2Ac
20	4	33.77 34.41 34.88 37.21	1567.6810 C ₇₂ H ₁₁₁ O ₃₇	1567.6818* 1567.6807 1567.6812 1567.6804	0.506 -0.196 0.117 -0.349	1567.6818 (45.4), 1525.6669 (0.9), 1507.6541 (2.7), 981.4710 (4.7), 939.4608 (100), 469.3320 (50.1)	G	Pent, Hex, HexA ^d	2dHex, Hex, Ac
21	2	39.07 40.17	1609.6915 C ₇₄ H ₁₁₃ O ₃₈	1609.6918* 1609.6930	0.148 0.906	1609.6918 (100), 1567.6704 (6.9), 1549.6744 (11.2), 1477.6443 (1.6), 1405.6355 (0.7), 981.4695 (3.8), 939.4605 (42.5), 565.3528 (20.1), 469.3322 (41.4), 423.3267 (2.6)	G	Pent, Hex, HexA ^d	2dHex, Pent, Hex, 2Ac
22	3	34.53 35.33 35.53	1699.7232 C ₇₇ H ₁₁₉ O ₄₁	1699.7223* 1699.7217 1699.7213	-0.550 -0.904 -0.909	1699.7223 (29.8), 1657.7091 (0.4), 1567.6846 (0.7), 1495.6663 (0.2), 981.4664 (0.2), 939.4602 (100), 565.3536 (9.1), 469.3321 (0.6), 423.3273 (0.5)	G	Pent, Hex, HexA ^d	2dHex, 2Pent, Hex, Ac
23	1	37.48	1699.7232 C ₇₇ H ₁₁₉ O ₄₁	1699.7289	3.327	1699.7289 (85.1), 955.4550 (57.4), 485.3252 (30.7), 405.3168 (31.2)	QA	Pent, Hex, HexA ^d	3dHex, 2Pent, Ac
24	4	40.24 40.27 41.02 41.20	1741.7338 C ₇₉ H ₁₂₁ O ₄₂	1741.7341* 1741.7313 1741.7332 1741.7339	-0.368 -1.418 -0.308 0.057	1741.7341 (100), 1723.7231 (1.0), 1699.7246 (0.9), 1609.6945 (0.5), 939.4600 (23.6), 565.3528 (9.3), 469.3320 (26.1), 423.3274 (2.8)	G	Pent, Hex, HexA ^d	2dHex, 2Pent, Hex, 2Ac
25	2	29.60 29.79	1771.7444 C ₈₀ H ₁₂₃ O ₄₃	1771.7430 1771.7438*	-0.740 -0.330	1771.7438 (7.5), 1753.7328 (0.9), 1729.7343 (0.8), 1639.7041 (1.9), 939.4670 (30.9), 565.3536 (48.9), 469.3329 (100), 423.3271 (9.5)	G	Pent, Hex, HexA ^d	2dHex, Pent, 2Hex, 2Ac
Bidesmosides with C-28 oligosaccharide substituted with methoxycinnamoyl group (type IV)									

26	2	44.76 45.89	1685.7228 C ₈₀ H ₁₁₇ O ₃₈	1685.7272* 1685.7217	2.574 -0.683	1685.7272 (36.2), 939.4626 (33.9), 469.3328 (100), 423.3298 (10.6), 177.0550 (2.4), 145.0288 (8.6), 117.0337 (9.2)	G	Pent, Hex, HexA ^d	2dHex, Pent, Hex, Mecin
27	4	45.09 45.28 46.20 46.37	1817.7651 C ₈₅ H ₁₂₅ O ₄₂	1817.7617* 1817.7623 1817.7628 1817.7629	-1.854 -1.519 -1.249 -1.183	1817.7617 (53.3), 939.4638 (42.4), 565.3541 (30.7), 469.3333 (100), 423.3260 (6.8), 145.0290 (4.0)	G	Pent, Hex, HexA ^d	2dHex, 2Pent, Hex, Mecin
28	4	48.37 48.60 49.34 49.54	1859.7757 C ₈₇ H ₁₂₇ O ₄₃	1859.7729* 1859.7727 1859.7728 1759.7736	-1.454 -1.584 -1.519 -1.126	1859.7729 (100), 1817.7529 (0.4), 1727.7187 (0.4), 939.4604 (36.0), 565.3535 (19.3), 469.3322 (51.6), 177.0542 (2.1), 145.0278 (4.0)	G	Pent, Hex, HexA ^d	2dHex, 2Pent, Hex, Ac, Mecin
Bidesmosides with C-28 oligosaccharide substituted with both sulfate and acetyl/methoxycinnamoyl groups (type V)									
29	1	36.27	1515.5955 C ₆₇ H ₁₀₃ O ₃₆ S	1515.5942	-0.846	1177.4985 (4.5), 707.1719 (100), 647.1520 (3.4), 607.1181 (13.5), 583.3657 (3.4), 579.1247 (15.3), 527.1638 (2.8), 519.1012 (44.6), 503.1071 (22.9), 469.3320 (3.1), 371.6641 (14.7), 329.0180 (8.9), 301.0225 (4.5), 259.0120 (18.9), 241.0018 (57.9)	G	Hex, HexA	dHex(C4-Ac), dHex, Pent, Hex (SO ₃ H)
30	1	34.30	1647.6378 C ₇₂ H ₁₁₁ O ₄₀ S	1647.6418	2.469	1647.6418 (32.0), 1567.6851 (1.9), 1177.5107 (11.9), 939.4605 (3.9), 707.1713 (100), 649.1298 (4.5), 621.1342 (3.3), 561.1132 (8.9), 469.3308 (1.0), 301.0236 (1.7)	G	Pent, Hex, HexA ^d	dHex(C3-Ac), dHex, Pent, Hex (SO ₃ H)
31	2	36.26 36.44	1647.6378 C ₇₂ H ₁₁₁ O ₄₀ S	1647.6415* 1647.6411	2.578 2.353	1647.6415 (95.5), 1567.6820 (15.3), 1485.5869 (0.2), 1177.5112 (74.1), 939.4614 (0.2), 707.1715 (100), 647.1500 (2.9), 607.1190 (7.5), 527.1611 (2.4), 519.1023 (2.7), 469.3324 (4.9), 371.0648 (2.1), 241.0016 (7.0)	G	Pent, Hex, HexA ^d	dHex(C4-Ac), dHex, Pent, Hex (SO ₃ H)
32	2	39.31 39.51	1689.6483 C ₇₄ H ₁₁₃ O ₄₁ S	1689.6506* 1689.6505	1.352 1.281	1689.6506 (96.3), 1609.6920 (14.4), 1219.5211 (72.9), 939.4621 (6.0), 749.1819 (100),	G	Pent, Hex, HexA ^d	dHex(C4-Ac), dHex, Pent, Hex (Ac,

						545.1183 (4.4), 469.3322 (4.5), 283.0131 (3.0)			SO ₃ H)
33	2	43.62 45.40	1765.6644 C ₇₆ H ₁₁₇ O ₄₄ S	1765.6783* 1765.6783	7.901 7.901	1765.6783 (100), 1685.7256 (19.1), 1295.5521 (77.7), 939.4604 (6.3), 825.2137 (89.1), 607.1147 (7.2), 527.1546 (0.4), 519.1021 (17.8), 503.1075 (4.4), 469.3321 (6.3), 423.3256 (8.3), 241.0017 (8.7), 177.0547 (0.3), 145.0280 (0.4)	G	Pent, Hex, HexA ^d	dHex(C4-Mecin), dHex, Pent, Hex(SO ₃ H)
34	1	36.24	1779.6789 C ₇₇ H ₁₁₉ O ₄₄ S	1779.6782	-1.023	1779.6782 (100), 1699.7242 (10.5), 1647.6282 (0.5), 1309.5521 (52.0), 939.4620 (2.6), 839.2134 (76.2), 659.2036 (1.3), 651.1481 (12.2), 635.1510 (5.5), 469.3310 (3.0), 241.0018 (5.4)	G	Pent, Hex, HexA ^d	dHex(C4-Ac), dHex, 2Pent, Hex(SO ₃ H)

*precursor ion - MS/MS fragment ions are described in the column "Fragmenttaion pattern in MS/MS"

^at_R – retention time

^baccurate mass (relative abundance)

^cG, gypsogenin; GA, gypsogenic acid; QA, quillaic acid; OA, oleanolic acid; Pent, pentose; Hex, hexose; dHex, deoxyhexose; HexA, hexuronic acid; SO₃H, sulphate group; Ac, acetyl group; Mecin, methoxycinnamoyl group

^dO-β-D-galactopyranosyl-(1→2)-[pentosyl-(1→3)]-β-D-glucuronopyranoside

Table S2. One-way ANOVA – *in vitro* cytotoxicity of GOTCAB saponins in HD-MY-Z cells at concentration of 20 µg/ml after 72 h of treatment.

Tukey's multiple comparisons test	Mean Difference	95% confidence interval of difference	Significance	Summary	Adjusted P Value*
Co vs. A1	5,000	-6,694 to 16,69	No	ns	0,8976
Co vs. A2	6,000	-5,694 to 17,69	No	ns	0,7590
Co vs. B1	14,00	2,306 to 25,69	Yes	**	0,0097
Co vs. B2	1,000	-10,69 to 12,69	No	ns	"> 0,9999"
Co vs. D1	-28,00	-39,69 to -16,31	Yes	****	"< 0,0001"
Co vs. D2	12,00	0,3064 to 23,69	Yes	*	0,0406
Co vs. E2	1,000	-10,69 to 12,69	No	ns	"> 0,9999"
Co vs. F2a	-9,000	-20,69 to 2,694	No	ns	0,2496
Co vs. F2b	-27,00	-38,69 to -15,31	Yes	****	"< 0,0001"
A1 vs. A2	1,000	-10,69 to 12,69	No	ns	"> 0,9999"
A1 vs. B1	9,000	-2,694 to 20,69	No	ns	0,2496
A1 vs. B2	-4,000	-15,69 to 7,694	No	ns	0,9721
A1 vs. D1	-33,00	-44,69 to -21,31	Yes	****	"< 0,0001"
A1 vs. D2	7,000	-4,694 to 18,69	No	ns	0,5785
A1 vs. E2	-4,000	-15,69 to 7,694	No	ns	0,9721
A1 vs. F2a	-14,00	-25,69 to -2,306	Yes	**	0,0097
A1 vs. F2b	-32,00	-43,69 to -20,31	Yes	****	"< 0,0001"
A2 vs. B1	8,000	-3,694 to 19,69	No	ns	0,3979
A2 vs. B2	-5,000	-16,69 to 6,694	No	ns	0,8976
A2 vs. D1	-34,00	-45,69 to -22,31	Yes	****	"< 0,0001"
A2 vs. D2	6,000	-5,694 to 17,69	No	ns	0,7590
A2 vs. E2	-5,000	-16,69 to 6,694	No	ns	0,8976
A2 vs. F2a	-15,00	-26,69 to -3,306	Yes	**	0,0045
A2 vs. F2b	-33,00	-44,69 to -21,31	Yes	****	"< 0,0001"
B1 vs. B2	-13,00	-24,69 to -1,306	Yes	*	0,0201
B1 vs. D1	-42,00	-53,69 to -30,31	Yes	****	"< 0,0001"
B1 vs. D2	-2,000	-13,69 to 9,694	No	ns	0,9998
B1 vs. E2	-13,00	-24,69 to -1,306	Yes	*	0,0201
B1 vs. F2a	-23,00	-34,69 to -11,31	Yes	****	"< 0,0001"
B1 vs. F2b	-41,00	-52,69 to -29,31	Yes	****	"< 0,0001"
B2 vs. D1	-29,00	-40,69 to -17,31	Yes	****	"< 0,0001"
B2 vs. D2	11,00	-0,6936 to 22,69	No	ns	0,0787
B2 vs. E2	0,0	-11,69 to 11,69	No	ns	"> 0,9999"
B2 vs. F2a	-10,00	-21,69 to 1,694	No	ns	0,1448
B2 vs. F2b	-28,00	-39,69 to -16,31	Yes	****	"< 0,0001"
D1 vs. D2	40,00	28,31 to 51,69	Yes	****	"< 0,0001"
D1 vs. E2	29,00	17,31 to 40,69	Yes	****	"< 0,0001"
D1 vs. F2a	19,00	7,306 to 30,69	Yes	***	0,0002
D1 vs. F2b	1,000	-10,69 to 12,69	No	ns	"> 0,9999"
D2 vs. E2	-11,00	-22,69 to 0,6936	No	ns	0,0787
D2 vs. F2a	-21,00	-32,69 to -9,306	Yes	****	"< 0,0001"
D2 vs. F2b	-39,00	-50,69 to -27,31	Yes	****	"< 0,0001"
E2 vs. F2a	-10,00	-21,69 to 1,694	No	ns	0,1448
E2 vs. F2b	-28,00	-39,69 to -16,31	Yes	****	"< 0,0001"
F2a vs. F2b	-18,00	-29,69 to -6,306	Yes	**	0,0004

Legend: *A P value lower than 0.05 was considered as significant difference.

Table S3. One-way ANOVA – *in vitro* cytotoxicity of GOTCAB saponins in CCL-1 cells at concentration of 20 µg/ml after 72 h of treatment.

Tukey's multiple comparisons test	Mean Difference	95% confidence interval of difference	Significance	Summary	Adjusted P Value*
Co vs. A1	2,626	-14,53 to 19,78	No	ns	> 0,9999
Co vs. A2	8,586	-8,568 to 25,74	No	ns	0,7710
Co vs. B1	21,72	4,563 to 38,87	Yes	**	0,0057
Co vs. B2	-3,788	-20,94 to 13,37	No	ns	0,9986
Co vs. D1	-6,566	-25,09 to 11,96	No	ns	0,9616
Co vs. D2	9,848	-8,680 to 28,38	No	ns	0,7092
Co vs. E2	28,38	11,23 to 45,54	Yes	***	0,0002
Co vs. F2a	4,394	-14,13 to 22,92	No	ns	0,9976
Co vs. F2b	-11,77	-30,30 to 6,761	No	ns	0,4862
A1 vs. A2	5,960	-11,19 to 23,11	No	ns	0,9660
A1 vs. B1	19,09	1,937 to 36,24	Yes	*	0,0205
A1 vs. B2	-6,414	-23,57 to 10,74	No	ns	0,9472
A1 vs. D1	-9,192	-27,72 to 9,336	No	ns	0,7793
A1 vs. D2	7,222	-11,31 to 25,75	No	ns	0,9330
A1 vs. E2	25,76	8,604 to 42,91	Yes	***	0,0007
A1 vs. F2a	1,768	-16,76 to 20,30	No	ns	> 0,9999
A1 vs. F2b	-14,39	-32,92 to 4,134	No	ns	0,2325
A2 vs. B1	13,13	-4,023 to 30,29	No	ns	0,2487
A2 vs. B2	-12,37	-29,53 to 4,780	No	ns	0,3190
A2 vs. D1	-15,15	-33,68 to 3,377	No	ns	0,1806
A2 vs. D2	1,263	-17,27 to 19,79	No	ns	> 0,9999
A2 vs. E2	19,80	2,644 to 36,95	Yes	*	0,0146
A2 vs. F2a	-4,192	-22,72 to 14,34	No	ns	0,9983
A2 vs. F2b	-20,35	-38,88 to -1,825	Yes	*	0,0231
B1 vs. B2	-25,51	-42,66 to -8,351	Yes	***	0,0008
B1 vs. D1	-28,28	-46,81 to -9,754	Yes	***	0,0006
B1 vs. D2	-11,87	-30,40 to 6,660	No	ns	0,4747
B1 vs. E2	6,667	-10,49 to 23,82	No	ns	0,9341
B1 vs. F2a	-17,32	-35,85 to 1,205	No	ns	0,0811
B1 vs. F2b	-33,48	-52,01 to -14,96	Yes	****	< 0,0001
B2 vs. D1	-2,778	-21,31 to 15,75	No	ns	> 0,9999
B2 vs. D2	13,64	-4,892 to 32,16	No	ns	0,2944
B2 vs. E2	32,17	15,02 to 49,33	Yes	****	< 0,0001
B2 vs. F2a	8,182	-10,35 to 26,71	No	ns	0,8705
B2 vs. F2b	-7,980	-26,51 to 10,55	No	ns	0,8857
D1 vs. D2	16,41	-3,394 to 36,22	No	ns	0,1684
D1 vs. E2	34,95	16,42 to 53,48	Yes	****	< 0,0001
D1 vs. F2a	10,96	-8,848 to 30,77	No	ns	0,6633
D1 vs. F2b	-5,202	-25,01 to 14,61	No	ns	0,9949
D2 vs. E2	18,54	0,006894 to 37,06	Yes	*	0,0499
D2 vs. F2a	-5,455	-25,26 to 14,35	No	ns	0,9928
D2 vs. F2b	-21,62	-41,42 to -1,808	Yes	*	0,0244
E2 vs. F2a	-23,99	-42,52 to -5,461	Yes	**	0,0045
E2 vs. F2b	-40,15	-58,68 to -21,62	Yes	****	< 0,0001
F2a vs. F2b	-16,16	-35,97 to 3,646	No	ns	0,1827

Legend: *A P value lower than 0.05 was considered as significant difference.

Table S4. Two-way ANOVA for generation of ROS in HD-MY-Z cells after treatment with ETP or combinations between ETP and 20 µg/ml saponin B2 or D2 for 6 h.

Tukey's multiple comparisons test	Mean Difference	95% confidence interval of difference	Significance	Summary	Adjusted P Value*
Co vs. 20 µg/mL B2	-16621	-46579 to 13338	No	ns	0,7650
Co vs. 20 µg/mL D2	-21925	-51883 to 8034	No	ns	0,3465
Co vs. 22.0 µg/ml ETP	-1092	-31051 to 28867	No	ns	> 0,9999
Co vs. 22.02 µg/ml ETP+20 µg/mL B2	-24044	-54002 to 5915	No	ns	0,2218
Co vs. 22.02 µg/ml ETP+20 µg/mL D2	-34577	-64535 to -4618	Yes	*	0,0136
Co vs. 44.18 µg/ml ETP	-15505	-45463 to 14454	No	ns	0,8417
Co vs. 44.18 µg/ml ETP+20 µg/mL B2	-44551	-74510 to -14592	Yes	***	0,0007
Co vs. 44.18 µg/ml ETP+20 µg/mL D2	-50828	-80787 to -20869	Yes	***	0,0001
Co vs. 88.35 µg/ml ETP	-15639	-45597 to 14320	No	ns	0,8332
Co vs. 88.35 µg/ml ETP+20 µg/mL B2	-76832	-106791 to -46873	Yes	****	"< 0,0001"
Co vs. 88.35 µg/ml ETP+20 µg/mL D2	-75802	-105760 to -45843	Yes	****	"< 0,0001"
Co vs. 176.7 µg/ml ETP	-19179	-49137 to 10780	No	ns	0,5578
Co vs. 176.7 µg/ml ETP+20 µg/mL B2	-61226	-91184 to -31267	Yes	****	"< 0,0001"
Co vs. 176.7 µg/ml ETP+20 µg/mL D2	-107734	-137693 to -77775	Yes	****	"< 0,0001"
Co vs. 353.4 µg/ml ETP	-51043	-81001 to -21084	Yes	***	0,0001
Co vs. 353.4 µg/ml ETP+20 µg/mL B2	-92547	-122506 to -62588	Yes	****	"< 0,0001"
Co vs. 353.4 µg/ml ETP+20 µg/mL D2	-118483	-148441 to -88524	Yes	****	"< 0,0001"
20 µg/mL B2 vs. 20 µg/mL D2	-5304	-33543 to 22935	No	ns	> 0,9999
22.02 µg/ml ETP vs. 22.02 µg/ml ETP+20 µg/mL B2	-22952	-52910 to 7007	No	ns	0,2211
22.02 µg/ml ETP vs. 22.02 µg/ml ETP+20 µg/mL D2	-33485	-63443 to -3526	Yes	*	0,0093
22.02 µg/ml ETP+20 µg/mL B2 vs. 22.02 µg/ml ETP+20 µg/mL D2	-10533	-40492 to 19426	No	ns	0,9943
44.18 µg/ml ETP vs. 44.18 µg/ml ETP+20 µg/mL B2	-29047	-57286 to -807,1	Yes	*	0,0390
44.18 µg/ml ETP vs. 44.18 µg/ml ETP+20 µg/mL D2	-35324	-63563 to -7084	Yes	**	0,0050
44.18 µg/ml ETP+20 µg/mL B2 vs. 44.18 µg/ml ETP+20 µg/mL D2	-6277	-36236 to 23682	No	ns	> 0,9999
88.35 µg/ml ETP vs. 88.35 µg/ml ETP+20 µg/mL B2	-61194	-91152 to -31235	Yes	****	"< 0,0001"
88.35 µg/ml ETP vs. 88.35 µg/ml ETP+20 µg/mL D2	-60163	-90122 to -30204	Yes	****	"< 0,0001"
88.35 µg/ml ETP+20 µg/mL B2 vs. 88.35 µg/ml ETP+20 µg/mL D2	1031	-28928 to 30989	No	ns	> 0,9999
176.7 µg/ml ETP vs. 176.7 µg/ml ETP+20 µg/mL B2	-42047	-70286 to -13808	Yes	***	0,0005
176.7 µg/ml ETP vs. 176.7 µg/ml ETP+20 µg/mL D2	-88556	-116795 to -60316	Yes	****	< 0,0001
176.7:ETP+20 µg/mL B2 vs. 176.7:ETP+20 µg/mL D2	-46509	-74748 to -18269	Yes	***	0,0001
353.4 µg/ml ETP vs. 353.4 µg/ml ETP+20 µg/mL B2	-41505	-69744 to -13265	Yes	***	0,0006
353.4 µg/ml ETP vs. 353.4 µg/ml ETP+20 µg/mL D2	-67440	-95679 to -39201	Yes	****	< 0,0001
353.4 µg/ml ETP+20 µg/mL B2 vs. 353.4 µg/ml ETP+20 µg/mL D2	-25936	-55894 to 4023	No	ns	0,0991

Legend: *A P value lower than 0.05 was considered as significant difference. The positive control was significantly different from all other groups of variances with $p < 0,0001$.

Table S5. Two-way ANOVA for activation of caspases in HD-MY-Z cells after treatment with ETP or combinations between ETP and 20 µg/mL saponin B2 or D2 for 6 h.

Tukey's multiple comparisons test	Mean Difference	95% confidence interval of difference	Significance	Summary	Adjusted P Value*
Co vs. 20 µg/mL B2	-792,5	-3646 to 2061	No	ns	"> 0,9999"
Co vs. 20 µg/mL D2	-1687	-4540 to 1167	No	ns	"> 0,9999"
Co vs. 22.0 µg/ml ETP	382,0	-2472 to 3236	No	ns	> 0,9999
Co vs. 22.02 µg/ml ETP+20 µg/mL B2	-176,0	-3030 to 2678	No	ns	"> 0,9999"
Co vs. 22.02 µg/ml ETP+20 µg/mL D2	-1238	-4092 to 1616	No	ns	0,9629
Co vs. 44.18 µg/ml ETP	-760,0	-3614 to 2094	No	ns	"> 0,9999"
Co vs. 44.18 µg/ml ETP+20 µg/mL B2	-2852	-5705 to 2,128	No	ns	0,0395
Co vs. 44.18 µg/ml ETP+20 µg/mL D2	-3193	-6046 to -338,9	Yes	*	0,0130
Co vs. 88.35 µg/ml ETP	-2025	-4878 to 829,1	No	ns	0,3796
Co vs. 88.35 µg/ml ETP+20 µg/mL B2	-4020	-6874 to -1166	Yes	**	"< 0,0001"
Co vs. 88.35 µg/ml ETP+20 µg/mL D2	-4145	-6999 to -1291	Yes	***	"< 0,0001"
Co vs. 176.7 µg/ml ETP	-3871	-6724 to -1017	Yes	**	0,0013
Co vs. 176.7 µg/ml ETP+20 µg/mL B2	-6575	-9429 to -3721	Yes	****	"< 0,0001"
Co vs. 176.7 µg/ml ETP+20 µg/mL D2	-7579	-10433 to -4725	Yes	****	"< 0,0001"
Co vs. 353.4 µg/ml ETP	-6541	-9394 to -3687	Yes	****	"< 0,0001"
Co vs. 353.4 µg/ml ETP+20 µg/mL B2	-9018	-11872 to -6164	Yes	****	"< 0,0001"
Co vs. 353.4 µg/ml ETP+20 µg/mL D2	-11754	-14607 to -8900	Yes	****	"< 0,0001"
20 µg/mL B2 vs. 20 µg/mL D2	-894,0	-3748 to 1960	No	ns	> 0,9999
22.02 µg/ml ETP vs. 22.02 µg/ml ETP+20 µg/mL B2	-558,0	-3412 to 2296	No	ns	"> 0,9999"
22.02 µg/ml ETP vs. 22.02 µg/ml ETP+20 µg/mL D2	-1620	-4474 to 1234	No	ns	0,7406
22.02 µg/ml ETP+20 µg/mL B2 vs. 22.02 µg/ml ETP+20 µg/mL D2	-1062	-3916 to 1792	No	ns	0,9923
44.18 µg/ml ETP vs. 44.18 µg/ml ETP+20 µg/mL B2	-2092	-4945 to 762,1	No	ns	0,3280
44.18 µg/ml ETP vs. 44.18 µg/ml ETP+20 µg/mL D2	-2433	-5286 to 421,1	No	ns	0,1384
44.18 µg/ml ETP+20 µg/mL B2 vs. 44.18 µg/ml ETP+20 µg/mL D2	-341,0	-3195 to 2513	No	ns	> 0,9999
88.35 µg/ml ETP vs. 88.35 µg/ml ETP+20 µg/mL B2	-2996	-5861 to -129,8	Yes	*	0,0248
88.35 µg/ml ETP vs. 88.35 µg/ml ETP+20 µg/mL D2	-3471	-6336 to -604,8	Yes	**	0,0051
88.35 µg/ml ETP+20 µg/mL B2 vs. 88.35 µg/ml ETP+20 µg/mL D2	-625,0	-3487 to 2237	No	ns	> 0,9999
176.7 µg/ml ETP vs. 176.7 µg/ml ETP+20 µg/mL B2	-3005	-5862 to -146,7	Yes	*	0,0241
176.7 µg/ml ETP vs. 176.7 µg/ml ETP+20 µg/mL D2	-3709	-6566 to -850,7	Yes	**	0,0022
176.7:ETP+20 µg/mL B2 vs. 176.7:ETP+20 µg/mL D2	-704,0	-3562 to 2154	No	ns	> 0,9999
353.4 µg/ml ETP vs. 353.4 µg/ml ETP+20 µg/mL B2	-2978	-5864 to -90,75	Yes	*	0,0263
353.4 µg/ml ETP vs. 353.4 µg/ml ETP+20 µg/mL D2	-5713	-8600 to -2826	Yes	****	"< 0,0001"
353.4 µg/ml ETP+20 µg/mL B2 vs. 353.4 µg/ml ETP+20 µg/mL D2	-3236	-6012 to -459,2	Yes	*	0,0112

Legend: *A P value lower than 0.05 was considered as significant difference. The positive control was significantly different from all other groups of variances with $p < 0,0001$

Table S6. One-way ANOVA for mono- and oligonucleosomes in the cytosole of HD-MY-Z cells after 48 h of treatment with ETP and combinations with saponins B2 and D2.

Tukey's multiple comparisons test	Mean Difference	95% confidence interval of difference	Significance	Summary	Adjusted P Value*
Control vs. ETP 22.02 µg/ml	-0,1658	-0,2762 to -0,05545	Yes	**	0,0028
Control vs. B2, 20 µg/ml	0,05794	-0,06545 to 0,1813	No	ns	0,6606
Control vs. D2, 20 µg/ml	-0,1397	-0,2631 to -0,01632	Yes	*	0,0232
Control vs. ETP + B2	-0,2906	-0,4010 to -0,1803	Yes	****	< 0,0001
Control vs. ETP + D2	-0,4104	-0,5207 to -0,3000	Yes	****	< 0,0001
ETP 22.02 µg/ml vs. B2, 20 µg/ml	0,2238	0,1004 to 0,3472	Yes	***	0,0005
ETP 22.02 µg/ml vs. D2, 20 µg/ml	0,02610	-0,09729 to 0,1495	No	ns	0,9867
ETP 22.02 µg/ml vs. ETP + B2	-0,1248	-0,2352 to -0,01446	Yes	*	0,0233
ETP 22.02 µg/ml vs. ETP + D2	-0,2445	-0,3549 to -0,1342	Yes	****	< 0,0001
B2, 20 µg/ml vs. D2, 20 µg/ml	-0,1977	-0,3328 to -0,06249	Yes	**	0,0035
B2, 20 µg/ml vs. ETP + B2	-0,3486	-0,4720 to -0,2252	Yes	****	< 0,0001
B2, 20 µg/ml vs. ETP + D2	-0,4683	-0,5917 to -0,3449	Yes	****	< 0,0001
D2, 20 µg/ml vs. ETP + B2	-0,1509	-0,2743 to -0,02753	Yes	*	0,0136
D2, 20 µg/ml vs. ETP + D2	-0,2706	-0,3940 to -0,1472	Yes	****	< 0,0001
ETP + B2 vs. ETP + D2	-0,1197	-0,2301 to -0,009351	Yes	*	0,0306

Legend: *A P value lower than 0.05 was considered as significant difference. The positive control was significantly different from all other groups of variances with $p < 0,0001$.