Supplementary materials

Characterization of Constituents with Potential Anti-Inflammatory Activity in Chinese Lonicera Species by UHPLC-HRMS Based Metabolite Profiling

Isolation procedure of OPLS-DA candidate compounds from *L. hypoglauca* methanolic extract

108 g of *L. hypoglauca* CH_3OH extract were suspended in 500 ml $CH_3OH:H_2O$ 9:1 and subjected to subsequent liquid-liquid extraction with 4x 500 ml n-hexane, 4x 500 ml ethyl acetate (EtOAc) and 4x 500 ml n-butanol. The extracts were dried in vacuo to yield 10.2 g *n*-hexane subextract, 25.5 g EtOAc subextract (EA), 16.2 g n-butanol subextract and 54 g H_2O residue.

25 g EA were subjected to VLC (vacuum liquid chromatography) on silica gel (300 g; column diameter 10 cm; stationary phase height 10 cm), using gradient elution with n-hexane- EtOAc – CH_3OH mixtures of increasing polarity. VLC eluates were combined based on similarities in their TLC profiles to achieve 8 subfractions (EA1-8). EA3 (*n*-hexane: EtOAc:CH_3OH 10:85:5, 2.55 g), EA4 (EtOAc:CH_3OH 90:10, 6.30 g) and EA5 (EtOAc:CH_3OH 90:10-75:25, 6.38 g) were separately dissolved in a mixture of CH_3OH and H_2O (9:1), and the solvent was gently evaporated by a rotary evaporator. As the CH_3OH concentration decreases by evaporation, lipophilic constituents precipitate and attach to the wall of the round bottom flask, while the other compounds stay in solution, allowing to separate the more polar subfractions EA3_1, EA4_1 and EA5_1 from the non-polar subfractions EA3_2, EA4_2 and EA5_2. EA3_1 and EA4_1 were combined to EAH (3.05 g), and EA4_2, EA5_2 as well as EA6 were combined to EAL (7.5 g).

EAL was subjected to further silica gel VLC fractionation (100 g; column diameter 7 cm, stationary phase height 6.5 cm) using gradient elution with CH_2Cl_2 - CH_3OH mixtures of increasing polarity. Eluates were combined to subfractions EAL_1-EAL-14. EAL_6 (CH_2Cl_2:CH_3OH 95:5-94:6, 560 mg) was purified by solid phase extraction (SPE) on a 5 g cartridge with $CH_3OH:H_2O$ mixtures (40:60-100:0). EAL6_6 ($CH_3OH:H_2O$ 90:10) was separated by semipreparative HPLC on a Shimadzu HPLC system, using a LiChrospher® 100, RP-18 (10 μm) LichroCART® 250-10, and HPLC column (Merck) as stationary phase. Column

temperature was 25 °C and $CH_3CN:H_2O$ 33:67 at a flow rate of 3 ml/min was used as mobile phase. Separation furnished compound **22** (1.8 mg).

EAL_10 ($CH_2Cl_2:CH_3OH$ 91:9-98:11, 437 mg) was purified on a 10 g SPE cartridge using $CH_3OH:H_2O$ mixtures (50:50-100:0). EAL_10_8 ($CH_3OH:H_2O$ 85:15, 39 mg) was separated by semipreparative HPLC on a Luna® C18 (2) 10 µm 100 Å LC column (10x250 mm) (Phenomenex) at a column temperature of 40 °C. The gradient of the mobile phase comprised of solvents A (H_2O + 0.2 % HCOOH) and B (CH_3CN/CH_3OH 7/3 + 0.2% HCOOH), where B in A is gradually increased from 75 to 95 % in 0-40 min at a flow rate of 5 ml/min. By this approach, we isolated compound **43** (0.8 mg) and compound **44** (1.0 mg).

EAL_11 ($CH_2Cl_2:CH_3OH$ 89:11, 280 mg) was purified too by a 10 g SPE cartridge using MeOH:H_2O mixtures (50:50-100:0). Purified subfraction EAL11_10 (MeOH:H_2O 95:5, 38 mg) was separated by semipreparative HPLC with the same conditions as for EAL_10_8, yielding 1.9 mg of compound **54**.

EAL_12 and EAL_13 were combined, and fraction EAL_12/13 ($CH_2Cl_2:CH_3OH$ 86:14-50:50, 2.24 g) was fractionated by another VLC on silica gel (100 g, column diameter 3.5 cm, stationary phase height 10 cm). Mixtures of $CH_2Cl_2:CH_3OH:H_2O$ with increasing polarity (90:10:1-60:40:4) served as mobile phase, resulting in 24 subfractions. Subfraction EAL12/13_15 ($CH_2Cl_2:CH_3OH:H_2O$ 85:15:1.5 340 mg) was further purified on a 10 g SPE cartridge using $CH_3OH:H_2O$ mixtures (50:50-100:0). Purified subfraction EAL12/13_15_8 (MeOH/H_2O 85:15, 39 mg) was separated by semipreparative HPLC using the same conditions as for EAL_10_8, furnishing further 0.5 mg of compound **43** and further 0.8 mg of compound **44,** and 6 mg of compound **46**. EAL12/13_15_9 (CH_3OH/H_2O 90:10, 80 mg) was separated according to the same semipreparative HPLC protocol, allowing to isolate another 2.6 mg of compound **54**. Taken together, 1.8 mg of compound **22**, 1.3 mg of compound **43**, 1.8 mg of compound **44**, 6.0 mg of compound **46** and 4.5 mg of compound **54** have been isolated from EAL.

EAH was further separated by column chromatography on RP-18 material (36 g, column diameter 5.2 cm, stationary phase height 3 cm), with a CH_3OH/H_2O gradient (10/90-90:10), resulting in subfractions EAH1-12. Subfraction EAH_11 (CH_3OH/H_2O 70:30-80:20, 104 mg) was separated by semipreparative HPLC on the Luna® C18 column (column temperature: 25°C, mobile phase: CH_3CN +0.1% HCOOH: H_2O +0.1% HCOOH 35:65; flow rate: 4.0 ml/min). By this method, we isolated compound **26** (1.8 mg), **27** (2.6 mg), and **29** (1.4 mg).

Supplementary Table S1: List of Lonicera samples included in the metabolic profiling study, their species assignment, collection date and origin, and extract yields obtained by ASE extraction with 96 % ethanol.

Sample ID	Species Name	Collection date	Origin	Yield (%) Aliquot_1	Yield (%) Aliquot_2
1_1, 1_2	*L. confusa* DC.	2011-11-07	Guangxi	16.65	16.88
2_1, 2_2	*L. hypoglauca* Miquel	2011-11-07	Guangxi	19.36	18.61
3_1, 3_2	*L. hypoglauca* Miquel	2011-11-07	Guangxi	17.53	17.08
4_1, 4_2	*L. confusa* DC.	2011-11-08	Guangxi	18.18	18.03
5_1, 5_2	*L. hypoglauca* Miquel	2011-11-08	Guangxi	20.21	20.21
6_1, 6_2	*L. confusa* DC.	2011-11-08	Guangxi	21.30	20.83
7_1, 7_2	*L. confusa* DC.	2011-11-08	Guangxi	19.99	19.55
8_1, 8_2	*L. similis* Hemsley	2011-11-07	Guangxi	13.15	13.17
9_1, 9_2	*L. hypoglauca* Miquel	2011-11-09	Guangxi	19.39	19.57
10_1, 10_2	*L. confusa* DC.	2011-11-09	Guangxi	26.10	24.49
11_1, 11_2	*L. confusa* DC.	2011-11-09	Guangxi	32.29	32.46
12_1, 12_2	*L. macrantha* (D. Don) Sprengel	2011-11-04	Guangxi	32.55	32.05
13_1, 13_2	*L. bournei* Hemsley	2011-11-05	Guangxi	39.61	40.29
14_1, 14_2	*L. hypoglauca* Miquel	2011-11-09	Guangxi	12.37	12.20
15_1, 15_2	*L. macrantha* (D. Don) Sprengel	2011-11-04	Guangxi	21.43	21.24
16_1, 16_2	*L. macrantha* (D. Don) Sprengel	2011-11-11	Guangxi	15.67	15.74
17_1, 17_2	*L. macrantha* (D. Don) Sprengel	2011-11-11	Guangxi	14.15	14.21

18_1, 18_2	L. similis Hemsley	2011-11-11	Guangxi	12.99	12.76
19_1, 19_2	*L. similis* Hemsley	2011-11-13	Guangxi	14.33	14.45
20_1, 20_2	*L. confusa* DC.	2011-11-13	Guangxi	6.88	6.39
21_1, 21_2	*L. macrantha* (D. Don) Sprengel	2011-11-15	Guangxi	8.73	8.91
22_1, 22_2	*L. reticulata* Champion	2011-11-05	Guangxi	24.19	24.27
23_1, 23_2	*L. japonica* Thunb.	2011-11-05	Guangxi	17.06	17.35
24_1, 24_2	*L. japonica* Thunb.	2011-11-07	Guangxi	8.59	8.40
25_1, 25_2	*L. japonica* Thunb.	2011-11-07	Guangxi	7.33	7.55
26_1, 26_2	*L. similis* Hemsley	2011-11-10	Guangxi	13.89	14.02
27_1, 27_2	*L. acuminata* Wallich	2011-11-11	Guangxi	17.30	19.77
28_1, 28_2	*L. reticulata* Champion	2011-11-13	Guangxi	14.60	14.41
29_1, 29_2	*L. acuminata* Wallich	2011-11-13	Guangxi	10.30	10.13
30_1, 30_2	*L. acuminata* Wallich	2011-11-13	Guangxi	18.97	18.43
31_1, 31_2	*L. macrantha* (D. Don) Sprengel	2011-11-13	Guangxi	10.01	10.17
32_1, 32_2	*L. acuminata* Wallich	2011-11-16	Guangxi	15.50	15.30
33_1, 33_2	*L. macrantha* (D. Don) Sprengel	2011-11-09	Guangxi	8.20	8.22
34_1	unidentified	2011-11-09	Guangxi	12.90	-
35_1, 35_2	*L. japonica* flower buds	NA	Purchased on TCM herb market	31.16	31.22
36_1, 36_2	*L. japonica* Thunb.	2011-05-30	Graz	14.17	14.47

Supplementary Table S2: Classification of *Lonicera* methanolic extracts according to the observed in vitro pharmacological activities.

Assay	Class	Activity	Readout	# samples
NO	1	Active	0-0.3 relative units	10
	2	Inactive	0.5->1 relative units	47
	3	Moderately active	0.3-0.5 relative units	14
NF-κB	1	High activity	0-0.1 relative units	42
	2	Low activity	0.3->1 relative units	9
	3	Moderate activity	0.1-0.3 relative units	20
IL-8	1	Active	0-0.3 relative units	15
	2	Inactive	0.5->1 relative units	42
	3	Moderately active	0.3-0.5 relative units	14

Supplementary Table S3: model window of PCA of preprocessed, normalized UHPLC-HRMS HESI negative ion mode data (score scatter plot [t1]/[t2] shown in Figure 1)

Component	R2X	R2X(cum)	Eigenvalue	Q2	Limit	Q2(cum)	Significance	Iterations
	Cent.							
1	0.147	0.147	10.4	0.114	0.0146	0.114	R1	53
2	0.126	0.272	8.94	0.114	0.0148	0.215	R1	34
3	0.0879	0.36	6.24	0.074	0.015	0.273	R1	68
4	0.0767	0.437	5.44	0.0639	0.0152	0.32	R1	84
5	0.0689	0.506	4.89	0.0817	0.0154	0.375	R1	28
6	0.0475	0.553	3.37	0.0371	0.0156	0.398	R1	200
7	0.0468	0.6	3.32	0.0482	0.0159	0.427	R1	41
8	0.0375	0.638	2.66	0.0291	0.0161	0.444	R1	93
9	0.0328	0.671	2.33	0.0278	0.0164	0.459	R1	93
10	0.0308	0.701	2.19	0.0368	0.0166	0.479	R1	90
11	0.0268	0.728	1.9	0.0127	0.0169	0.486	R2	122
12	0.0248	0.753	1.76	0.03	0.0171	0.501	R1	110
13	0.0231	0.776	1.64	-0.00254	0.0174	0.5	R2	67
14	0.0203	0.796	1.44	0.0378	0.0177	0.519	R1	85

Supplementary Table S4: Annotation of candidate compounds

Compounds shown in italics have been isolated from *L. hypoglauca* and their structure has been fully or partially elucidated by NMR spectroscopy; [a]Nr: Identified compounds are numbered in the same way as in Table 2; unidentified compounds or adducts of identified compounds are not numbered; [b]RT: retention time in minutes; [c]*m/z*: *m/z* of the base peak, used for molecular formula prediction; [d]*m/z* (adduct): *m/z* of adduct used for LDA verification; [e]MS/MS: *m/z* values of MS/MS fragments (% of base peak intensity); priority: deduced from S-plots of respective OPLS-DA models; low number represents high priority; numbers written in grey represent candidates with low reliability (jack-knife based confidence interval including 0); ID levels [1][2]: 0, isolated pure compound, unambiguous 3D structure; 1, confident 2D structure, identified by reference standard match (retention time and MS/MS); 2, tentative annotation by comparison of structural formula and MS/MS fragmentation pattern with data from databases or literature. 3, no data available in literature or databases; compound tentatively assigned on the basis of the MS/MS fragmentation pattern (theoretical interpretation and/or comparison to related compounds); 4, unknown feature of interest;   [f] structure additionally verified by Lipid Data analyzer (LDA)[3],[4]; Phospholipid and sphingolipid nomenclature, see [5]

Nr[a]	Monoiso-topic mass	RT[b]	*m/z*[c]	*m/z* (adduct)[d]	MS/MS[e]	Molecular formula	Δ (ppm)	IL8 priority	NFkB priority	NO priority	extract with high abundance (> average+2 S.D. in Xvar plot)	Annotation [iD level]	Reference
1	180.0423	10.71	179.0333		179.0333 (25) 135.0433 (100)	C9H8O4	-3.49		8		23_1, 23_2	caffeic acid [2]	MZCloud [No 337]
	676.20000	11.81	675.1924		675.1918 (15) 327.0873 (10) 191.0550 (100) 173.0443 (10)	C32H36O16	0.09			19	18_1, 18_2	unknown quinic acid derivative [4]	
2	338.1002	12.63	337.0924		173.0441 (100) 163.0386 (25) 155.0334 (10) 137.0227 (10) 119.0486 (15) 93.0328 (15)	C16H18O8	1.74			12	7_1, 7_2; 9_1, 9_2; 18_1, 18_2	coumaroylquinic acid [2]	literature [6]
3	338.1002	13.42	337.0925		191.0549 (100) 173.0442 (15) 163.0387 (15) 93.0329 (20) 87.0070 (10)	C16H18O8	2.19			20	9_1, 9_2; 18_1, 18_2	coumaroylquinic acid [2]	literature [6]

No	[M+H]⁺	RT	[M-H]⁻		MS/MS fragments m/z (%)	Formula	ppm					Codes	Identification	Reference
4	404.1319	15.62	403.1241		371.0993 (10) 165.0543 (25) 139.0023 (15) 123.0436 (15) 121.0279 (100) 113.0229 (15) 101.0228 (45) 95.0486 (30) 89.0227 (45) 71.0122 (40) 69.0329 (25) 59.0122 (50)	C17H24O11	1.54	9				35_1, 35_2; 36_1, 36_3	Secoxyloganin [1]	authentic reference
5	610.1534	18.27	609.1454		609.1456 (25) 447.0958 (5) 285.0401 (100)	C27H30O16	0.72		30			11_1, 11_2; 15_1, 15_2	luteolin-dihexoside [2]	literature [7] MSⁿ experiments
6	580.1428	19.99	579.1335		579.1339 (25) 447.0884 (1)	C26H28O15	1.66	10		13		23_1, 23_2; 30_1, 30_2	luteolin hexoside pentoside [2]	literature [7] MSⁿ experiments
7	448.101	20.91	447.0918		447.0920 (40) 285.0396 (100) 284.0318 (25)	C21H20O11	-0.93		27			23_1, 23_2	luteolin-7-glucoside [1]	authentic reference
8	594.1585	21.59	593.1501		593.1511 (15) 447.0928 (35) 431.0975 (35) 430.0897 (75) 285.0400 (100) 284.0323 (10) 283.0244 (90)	C27H30O15	-0.01		15		2	2_1, 2_2; 18_1, 18_2	kaempferol-3-hexoside-7-deoxyhexoside [2]	literature [8], [9] MSⁿ experiments
9	478.1111	21.99	477.1036		477.1035 (50) 462.0803 (100) 315.0510 (75) 300.0273 (50) 299.0197 (70) 271.0238 (10)	C22H22O12	1.74				26	5_1, 5_2	isorhamnetin-7-O-hexoside [2]	literature [10]
10	594.1585	22.00	593.1499		593.1501 (100) 447.0918 (10) 285.0398 (85) 284.0320 (50)	C27H30O15	-0.33	25				25_1, 25_2	lonicerin (luteolin hexoside deoxyhexoside) isomer [2]	literature [11], [12] MSⁿ experiments

#		RT			Fragments m/z (%)	Formula	Error (ppm)				Peak IDs	Identification	Reference
11	516.1268	22.19	515.1885		353.0873 (45) 191.0549 (100) 179.0337 (80) 173.0442 (25) 161.0230 (20) 135.0435 (20)	C25H24O12	0.13	24			15_1, 30_2, 33_1	dicaffeoylquinic acid ²	literature [13]
	758.2633	23.38	757.2536		689.3260 (5), 525.1597 (55) 493.1704 (15) 293.0659 (10) 261.0389 (15) 233.0450 (10) 181.0489 (15) 119.0330 (35) 113.0225 (40)101.0226 (100) 89.0226 (100) 85.0279 (10) 71.0210 (80) 59.0121 (100)	C34H46O19	-1.79	33			35_1	UNKNOWN ⁴	
12	516.1268	24.18	515.1176		353.0867 (25) 191.0547 (30) 179.034 (75) 173.0439 (100) 135.0434 (15)	C25H24O12	-1.53		11		32_1, 32_2	dicaffeoylquinic acid ²	literature [13]
13	448.1006	25.16	447.0924		447.0926 (35) 285.0400 (25) 284.0322 (100) 255.0292 (30) 227.0340 (15)	C21H20O11	0.56		2		19_1, 19_2	kaempferol-3-hexoside (astragalin isomer) ²	literature[14], [12] MSn experiments
14	478.1111	25.50	477.1035		477.1035 (50) 314.0431 (100) 299.0199 (10) 285.0403 (15) 271.0247 (20) 257.0454 (5) 243.0294 (15)	C22H22O12	1.61			30	5_1, 5_2	isorhamnetin-3-O-hexoside ²	literature [10], [15], [16]

#	Measured	RT	[M-H]⁻		Fragments (% intensity)	Formula	Error				Related	Compound	Identification
15	484.1369	26.69	483.1294		337.0927 (5) 319.0820 (10) 191.0552 (20) 173.0443 (25) 163.0388 (100) 145.0281 (5) 119.0487 (25)	C25H24O10	1.77			22	3_1, 3_2; 5_1, 5_2	3,5-di-O-p-coumaroylquinic acid [2]	literature [17]
16	610.1323	28.94	609.1244		609.1243 (30) 447.0934 (5) 323.0766 (5) 285.0401 (100) 179.0338 (5) 161.0230 (15)	C30H26O14	0.83			29	9_1, 9_2	luteolin-O-caffeoyl-O-hexoside [3]	Fragmentation and MSⁿ experiments
17	484.1369	29.84	483.1290		337.0926 (15) 191.0550 (5) 137.0230 (5) 119.0487 (5) 173.0442 (100) 163.0387 (25)	C25H24O10	0.83			16	7_1, 7_2; 18_1, 18_2	4,5-di-O-p-coumaroylquinic acid [2]	literature [17]
18	286.0477	30.06	285.040		285.0400 (100) 151.0021 (5) 133.0279 (5)	C15H10O6	2.26	28	3		15_1, 15_2; 25_1, 25_2	luteolin [1]	authentic reference
19	316.0583	30.89	315.0506		315.0505 (25) 300.0269 (100) 272.0320 (5) 151.0021 (10)	C16H12O7	2.13	39		21	14_1, 14_2	isorhamnetin [2]	MoNA [spectrum FiehnHILIC001279]
	536.1894	31.15	535.1810		535.1799 (5) 373.1280 (5) 341.1019 (10) 313.1075 (10) 209.0809 (10) 163.0386 (100) 119.0485 (30) 101.0227 (25)	C26H232O12	0.05		34		19_1, 19_2	UNKNOWN [4]	
20	594.1373	31.73	593.1294		593.1295 (35) 447.0928 (5) 285.0400 (100) 163.0383 (3) 145.0280 (10)	C30H26O13	0.71			27	9_1, 9_2	luteolin-O-coumaroyl-O hexoside [3]	Fragmentation and MSⁿ experiments

#	m/z	RT	[ion]		MS/MS fragments	Formula	error				Sample	Compound	Identification
21	270.0528	32.50	269.0452		269.0452 (100) 225.0548 (10) 151.0022 (10) 149.0225 (5) 117.0328 (5)	C15H10O5	2.68		25		15_1, 15_2	apigenin [1]	authentic reference
22	*358.105*	*32.64*	*357.098*		*357.0980 (45) 342.0743 (60) 327.0509 (100) 313.0718 (10) 299.0561 (20)*	*C19H18O7*	*3.03*	*8*		*7*	*5_1, 5_2; 14_1, 14_2*	*7-hydroxy-5,3´,4´,5´-tetramethoxyflavone [1]*	*isolated & identified*
23	300.0634	32.79	299.0555		299.0555 (30) 284.0320 (100) 256.0370 (5)	C16H12O6	1.56		26		25_1, 25_2	diosmetin/ chrysoeriol [2]	MoNA [spectrum Spectrum VF-NPL-QEHF014481/Meta boBASE0344]
	584.0955	32.89	583.0881		583.0880 (50) 568.0641 (50) 539.0956 (5) 497.0888 (10) 421.0568 (15) 417.0614 (20) 406.0330 (30) 375.0509 (100) 333.0406 (5) 257.0074 (10) 207.0287 (15) 192.0052(20) 163.0386 (5)	C31H20O12	0.82			23	5_1, 5_2; 14_1, 14_2	UNKNOWN [4]	
24	328.225	33.76	327.2169		327.2168 (100) 291.1952 (15) 239.1278 (10) 229.1434 (45) 221.1170 (15) 211.1327 (60) 183.1377 (10) 171.1010 (70) 137.0955 (10) 97.0641 (10) 85.0277 (25)	C18H32O5	-0.70		23		31_1, 31_2	trihydroxyocta-decadienoic acid isomer I [2]	literature [18]

No.	mass	RT	m/z	MS/MS fragments	formula	error (ppm)				detected in samples	compound	identification
25	328.2250	33.98	327.2169	327.2169 (100) 291.1957 (15) 239.1279 (10) 229.1435 (55) 221.1171 (15) 211.1327 (80) 183.1377 (10) 171.1010 (25) 97.0641 (10) 85.0277 (10)	C18H32O5	-0.70	19	1		29_1, 29_2; 31_1, 31_2	trihydroxyoctadecadienoic acid isomer II [2]	literature [18]
26	538.0900	35.07	537.0825	537.0823 (35) 443.0406 (15) 417.0614 (30) 399.0504 (15) 375.0506 (100)	C30H18O10	1.56		17	1	5_1, 5_2; 14_1, 14_2	cupressuflavone [0]	isolated & identified
27	568.1006	35.29	567.0928	567.0930 (100) 473.0503 (15) 447.0719 (25) 403.0407 (15) 417.0623 (20) 405.0614 (70) 390.0381 (35) 375.0508 (100)	C31H20O11	1.13		24	8	5_1, 5_2; 14_1, 14_2	3´-methoxycupressuflavone [0]	isolated & identified
28	330.2406	35.43	329.2325	329.2325 (100) 311.2224 (5) 293.2117 (5) 229.1435 (45) 211.1327 (65) 193.1217 (5) 183.1376 (10) 171.1011 (30) 139.1112 (10) 178.1110 (5) 99.0798 (10)	C18H34O5	-0.88		32		29_1, 29_2	trihydroxyocta-decenoic acid [2]	literature [18]
29	598.1111	35.51	597.1036	597.1038 (80) 473.0500 (10) 447.0724 (25) 405.0614 (100) 390.0381 (50)	C32H22O12	1.49	36	20	10	5_1, 5_2; 14_1, 14_2	3´, 3´´-dimethoxycupressuflavone [0]	isolated & identified

	306.1831	35.91	305.1751		305.1752 (25) 249.1487 (75) 205.1586 (15) 135.0798 (100) 125.0955 (20) 1234.0795 (10) 121.0640 (5) 97.0640 79.0534 (5) 71.0485 (19	C18H26O4	-0.67		33		20_1, 20_2; 31_1, 31_2	UNKNOWN [4]	
		36.91 2	1041.486 3 [M+CF₃CO O]⁻		671.3763 (15) 603.3882 (20) 112.9838 (100)	C49H76O20 F3	-1.63	29			1_1, 2_2; 30_1, 30_2	TFA adduct of akebiasaponin D (30) [3]	
30	**928.5032**	**36.92**	**927.4937**		**603.3904 (100)** **323.1013 (2)**	**C47H76O18**	**1.76**	**2**			**1_1, 1_2; 30_1, 30_2**	**Akebia saponin D [2]**	**literature [19], [20]**
31	**444.2049**	**36.99**	**443.1969**		**383.1758 (15)** **353.1624 (3)** **292.1215 (5)** **262.1239 (10)** **248.0948 (10)** **222.0913 (5)** **201.0658 (5)** **120.0431 (15)** **59.0122 (100)**	**C27H28O4N 2**	**-0.48**		**9**		**21_1, 21_2; 25_1, 25_2**	**aurantiamide acetate [2]**	**literature [21]**
	1076.180 0	37.22 7	1075.169 8 [2M-H]⁻		537.0812 (100) 443.0395 (20) 417.0606 (25) 375.0500 (75)	C60H36O20	-2.2		28		21_2; 31_1	amentoflavone dimer	
32	**538.0900**	**37.24**	**537.0817**		**537.0815 (50)** **443.0398 (25)** **417.0609 (35)** **399.0500 (20)** **375.0504 (100)** **331.0608 (15)** **203.0343 (3)** **159.0436 (5)** **117.0328 (5)**	**C30H18O10**	**-0.93**		**4**	**31**	**(20_1), 20_2**	**amentoflavone [1]**	**authentic reference**

No		RT	[M-H]⁻		MS/MS fragments	Formula	ppm				Assignment	Compound	Reference
33	552.1056	40.28	551.0975		551.0976 (30) 375.0505 (100) 331.0607 (10) 307.0608 (3) 173.0597 (5)	C31H20O10	-0.53		18	25	9_1, 9_2; 26_1, 26_2	podocarpusflavone A [1]	authentic reference
34	538.0900	40.96	537.0808		537.0811 (100) 493.0918 (5) 469.0914 (10) 385.0700 (5) 285.0396 (3) 284.0320 (5) 269.0450 (3) 151.0018 (5)	C30H18O10	-2.54		12		32_1, (32_2)	hinokiflavone [2]/ochnaflavone [2]	literature [22]
35	538.0900	41.43	537.082		537.0817 (100) 493.0919 (5) 469.0921 (10) 385.0711 (5) 285.0396 (2) 284.0324 (5) 269.0453 (3) 151.0020 (5)	C30H18O10	-0.38		29		19_1, 19_2; 29_1, 29_2	hinokiflavone [2]/ochnaflavone[2]	literature [22]
36	294.4298	41.93	293.2117		293.2116 (75) 275.2011 (100) 235.1694 (60) 231.2119 (10) 211.1330 (10) 195.1378 (7) 183.1377 (35) 177.1633 85) 171.1011 (35) 121.1006 (25)	C18H30O3	2.8		5		25_1, 25_2; 31_1, 31_2	oxo-octadecadienoic acid [2]	literature [23]
37	766.4503	41.95	765.4404		765.4413 (70) 603.3382 (100) 585.3773 (25) 525.3582 (5) 471.3465 (50) 423.3230 (10) 113.0227 (10) 101.0226 (20) 59.0121 (20)	C41H66O13	-2.81	34			1_1, 1_2; 30_1, 30_2	Akebia saponin C [2]	literature [24]

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38	604.3975	42.77	603.3885		603.3885 (100) 427.2431 (1) 391.8430 (1)	C35H56O8	-1.99	16			1_1, 1_2; 30_1, 30_2	Akebia saponin PA [2]	literature [24]
39	676.3670	43.50	721.3638 [M+HCOO]-		415.1450 (15) 397.1338 (20) 277.2164 (100) 253.0917)5) 235.0813 (15) 179.0541 (5) 161.0436 (5) 143.0331 (5) 125.0225 (10) 119.0330 (10) 101.0226 (30) 89.0226 (25) 71.0121 (20) 59.0121 (30)	C33H56O14	-0.72	26			30_2; 36_1, 36_2	gingerglycolipid A isomer [2]	literature [25]
40	517.3168	44.07	562.3136 [M+HCOO]-	562.314 [M+HCOO]-; 502.29 [M-CH3]-	502.2927 (15) 277.3264 (100) 224.0685 (15)	C26H48NO7P	-1.59	23			25_1; 29_1; 30_2	LPC 18:3 [2,f]	MoNA [spectrum LipidBlast454264]; LDA[3] (supplementary figure S7)
	372.3240	46.83	371.3154		371.3154 (40) 353.3055 (5) 311.2944 (20) 183.1738 (5) 59.0121 (100)	C22H44O4	-1.82	3			35_1	UNKNOWN [4]	
41	602.4758	47.19	601.4681		601.4683 (40) 541.4470 (5) 499.4365 (20) 115.0747 (5) 59.0123	C34H66O8	0.33	5	14	4	5_1, 5_2; 14_1, 14_2	trihydroxy-monoacetoxy-dotriacontanoic acid I [3]	n.a.
42	602.4758	47.55	601.4682		601.4684 (60) 583.4583 (10) 541.4466 (10) 499.4361 (25) 427.3806 (3) 297.2806 (3) 241.8599 (3)	C34H66O8	0.43	15		13	5_1, 5_2; 14_1, 14_2	trihydroxy-monoacetoxy-dotriacontanoic acid II [3]	n.a.

#													
					115.0748 (5) 59.0123 (100)								
43	*644.4860*	*47.96*	*643.4689*		*643.4792 (25)* *601.4709 (3)* *583.4568 (10)* *523.4394 (3)* *499.4388 (10)* *299.4382 (2)* *59.0123 (100)*	*C36H68O9*	*0.58*	6	22	5	*5_1, 5_2; 14_1, 14_2*	*trihydroxy-diacetoxy-dotriacontanoic acid I* [2]	*isolated & partly identified*
	400.3553	48.09	399.3467		399.3467 (45) 381.3349 (5) 339.2357 (20) 59.0121 (100)	C24H48O4	-0.44	22			35_1; 36_1, 36_2	UNKNOWN [4]	
44	*644.4860*	*48.24*	*643.4788*		*643.4790 (35)* *625.4689 (5)* *583.4576 (15)* *523.4355 (2)* *499.4371 (10)* *283.2639 (2)* *115.0747 (2)* *59.0123 (100)*	*C36H68O9*	*0.39*	17	31	9	*5_1, 5_2; 14_1, 14_2*	*trihydroxy-diacetoxy-dotriacontanoic acid II* [2]	*isolated & partly identified*
45	482.2645	48.42	481.2559		481.2551 (35) 253.2163 (35) 245.0422 (100) 227.0315 (15) 152.9941 (100) 78.9571 (10)	C22H42O9P	-0.37	35			25_1, 25_2; 30_1, 30_2	LPG 16:1 [2]	literature [26]
46	*644.4860*	*48.45*	*643.4786*		*643.4788 (30)* *601.4670 (5)* *583.4584 (10)* *499.4364 (10)* *481.4247 (3)* *59.0122 (100)*	*C36H68O9*	*0.11*	11	6	3	*5_1, 5_2; 14_1, 14_2*	*trihydroxy-diacetoxy-dotriacontanoic acid III* [2]	*isolated & partly identified*
47	630.5071	48.60	629.4995		629.4994 (45) 611.4891 (3) 569.4760 (10) 527.4674 (20) 115.0748 (5) 59.0123 (100)	C36H70O8	1.20	32		14	5_1, 5_2; 14_1, 14_2	tetrahydroxy-monoacetoxy-tetratriacontanoic acid I [3]	n.a.

48	556.2906	48.91	556.2917		555.2827 (100) 299.0062 (25) 164.0847 (10) 94.9791 (5) 80.9634 (15)	C25H48O11S	-0.72		21		25_1; 30_2	palmitoyl-sulfoquinovosyl-glycerol [2]	literature [27]
49	630.5071	48.96	629.4994		629.4995 (50) 611.4905 (5) 569.4794 (10) 527.4677 (20) 509.4564 (3) 325.3122 (3) 253.2528 (3) 187.1324 (3) 115.0750 (5) 59.0123 (100)	C36H70O8	1.10	13		11	5_1, 5_2; 14_1, 14_2	tetrahydroxy-monoacetoxy-tetratriacontanoic acid II [3]	n.a.
50	686.4969	49.16	685.4894		685.4892 (20) 643.4768 (5) 625.4685 (10) 583.4575 (3) 565.4472 (5) 499.4341 (3) 59.0122 (100)	C38H70O10	1.34	40		18	5_1, 5_2	dihydroxy-triacetoxy-dotriacontanoic acid [3]	n.a.
51	672.5176	49.24	671.5097		671.5100 (35) 653.5009 (3) 611.4897 (10) 551.4673 (3) 527.4663 (5) 59.0122 (100)	C38H72O9	0.57			17	3_1, 3_2; 5_1, 5_2; 14_1, 14_2	trihydroxy-diacetoxy-tetratriacontanoic acid I [3]	n.a.
52	592.2686	49.32	591.2602		515.2440 (100) 500.220(25) 497.2335 (7) 487.2531 (7) 443.2235 (3)	C35H36N4O5	-0.01		7		25_1, 25_2; 31_1, 31_2	pheophorbide A [1]	authentic reference
53	672.5176	49.52	671.5103		671.5100 (40) 653.5009 (3) 611.4897 (10) 551.4673 (3) 527.678 (5) 311.2943 (3) 59.0122 (100)	C38H72O9	1.47	31		15	3_1, 3_2; 5_1, 5_2; 14_1, 14_2	trihydroxy-diacetoxy-tetratriacontanoic acid II [3]	n.a.

#	m/z	RT	m/z (found)		MS/MS fragments	Formula	ppm				Positions	Name	Identification
54	*672.5176*	*49.75*	*671.5101*		*671.5104 (25)* *629.5004 (3)* *611.4898 (10)* *527.4669 (10)* *59.0123 (100)*	*C38H72O9*	*1.3*		*10*	*6*	*3_1, 3_2; 5_1, 5_2; 14_1, 14_2*	*trihydroxy-diacetoxy-tetratriacontanoic acid III [2]*	*isolated and partly identified*
55	484.2801	49.77	483.272		483.2719 (15) 255.2322 (100) 227.0315 (5) 152.9942 (25) 78.9572 (5)	C22H44O9P	0.46	7			25_1, 25_2; 29_2; 36_1, 36_2	LPG 16:0 [2]	literature [26]
56	714.5282	50.34	713.5208		713.5201 (20) 671.5075 (5) 653.5010 (10) 593.4786 (5) 527.4651 (3) 59.0122 (100)	C40H74O10	1.38			24	3_1, 3_2; 5_1, 5_2; 14_1, 14_2	dihydroxy-triacetoxy-tetratriacontanoic acid [3]	n.a.
	700.5489	50.86	699.5407		699.5401 (30) 639.5221 (10) 555.4976 (10) 59.0122 (100)	C40H76O9	0.21			28	3_1, 3_2; 5_1, 5_2; 14_1, 14_2	UNKNOWN [4]	
57	713.5435	51.99	712.5349		712.5335 (15) 550.4824 (35) 532.4717 (45) 306.2426 (10) 295.2581 (25) 278.2468 (25) 253.2148 (15) 225.2213 (35) 119.0334 (25) 113.0226 (35) 101.0227 (65) 89.0226 (85) 71.0120 (70) 59.0121 (100)	C40H75O9N	-2.03	21			1_1, 1_2	soyacerebroside (HexCer 18:2;O2/16:0;O) [2]	literature [23], [28]
58	384.3603	52.47	383.3535		383.3523 (100) 365.3411 (3) 337.3470 (75)	C24H48O3	1.4		19		24_1, 24_2	hydroxytetracosanoic acid [2]	literature [29]
		53.94	473.2813		473.2811 (100) 457.2520 (3) 205.1589 (3)	?		27			36_1, 36_2	UNKNOWN [4]	

#	m/z	RT		Ion	MS/MS fragments	Formula	ppm					Identification	Reference
59	669.5907	54.33	668.5819	668.580 [M-H]⁻; 714.590 [M+HCOO]⁻	668.5800 (20) 372.2744 (100) 354.2632 (10) 336.2557 (10) 306.2430 (15) 265.2164 (35) 253.2159 (10) 130.0492 (85) 118.0491 (100) 100.0386 (30) 75.0070 (70)	C40H79O6N	-0.77	39			33_1, 33_2; 36_1, 36_2	Cer 18:1; O3/22:0;O2 [2,f]	literature [30], LDA[4] (supplementary figure S8)
		55.43	766.5795 [M+CF3COO]-		112.9837 (100) 68.9940 (50)	C42H79O7NF3	-1.1	18			30_1; 34_1; 36_1, 36_2	TFA adduct of 60 [3]	
60	653.5958	55.44	652.5867	652.590 [M-H]⁻ 688.560 [M+Cl]⁻	652.5869 (90) 634.5752 (5) 410.3625 (35) 398.3631 (50) 380.3522 (15) 355.3208 (90) 337.3098 (20) 309.3154 (100) 282.2429 (10) 265.2161 (25) 253.2167 (35) 223.2051 (10) 88.0386 (10)	C40H79O5N	-1.11	14			1_1, 1_2; 34_1	Cer 18:1;O3/22:0;O [2,f]	literature [30], LDA[4] (supplementary figure S9)
61	697.6220	55.60	696.6129	696.610 [M-H]⁻; 742.619 [M+HCOO]⁻ ;	696.6117 (20) 372.2746 (100) 354.2651 (10) 336.2528 (15) 306.2430 (20) 265.2165 (35) 253.21654 (15) 130.0492 (85) 118.0492 (100)100.0386 (30) 75.0099 (80)	C42H83O6N	-1.07	4	16		33_1, 33_2; 36_1, 36_2	Cer18:1;O3/24:0;O2 [2, f]	literature [30], LDA[4] (supplementary figure S10)

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	810.6071	55.60	810.6058 [M+CF3COO]-		112.9837 (100) 68.9940 (50)	C44H83O8NF3	-0.94	12	35		25_1, 25_2; 33_1, 33_2; 36_1, 36_2	TFA adduct of 61 [3]	
62	667.6115	56.15	780.5953 [M+CF3COO]-	666.600 [M-H]-; 712.610 [M+HCOO]-; 702.580 [M+Cl]-	666.6024 (100) 648.5941 (10) 424.3790 (40) 412.3785 (50) 394.3656 (15) 369.3362 (95) 351.3263 (20) 323.3309 (100) 282.2424 (15) 265.2163 (25) 253.2163 (35) 223.2056 (10) 88.0387 (15)	C41H81O5N	-1.02	30			25_1, 25_2; 30_2; 36_1, 36_2	Cer 18:1;O3/23:0;O [2,f]	literature [30], LDA[4] (supplementary figure S11)
63	681.6271	56.95	680.6178	680.620 [M-H]-; 726.624 [M+HCOO]-; 716.598 [M+Cl]-	680.6177 (85) 438.3945 (35) 426.3944 (45) 383.3522 (90) 365.3412 (20) 337.3467 (100) 282.2436 (10) 265.2167 (25) 253.2163 (35) 88.0387 (10)	C42H83O5N	-1.4	1			1_1, 1_2	Cer18:1;O3/24:0;O [2,f]	literature [30], LDA[4] (supplementary figure S12)
64	683.6428	57.83	796.6273 [M+CF3COO]-	682.630 [M-H]-; 728.640 [M+HCOO]-; 718.610 [M+Cl]-	682.6344 (100) 438.3947 (25) 426.3950 (45) 383.3524 (80) 365.3428 (15) 337.3471 (100) 284.2592 (10) 267.2326 (25) 255.2320 (30) 225.2214 (5) 88.0387 (10)	C42H85O5N	-0.36	20			25_1, 25_2; 36_1, 36_2	Cer18:0;O3/24:0;O [2,f]	literature [30], LDA [4] (supplementary figure S13)

| 65 | 709.6584 | 58.85 | 822.6422 [M+CF3COO]- | 708.650 [M-H]⁻; 754.650 [M+HCOO]⁻; 744.627 [M+Cl]⁻ | 708.6490 (95) 690.6365 (5) 466.4243 (35) 454.4252 (55) 436.4153 (10) 411.3831 (90) 393.3730 (15) 365.3776 (100) 282.2426 (10) 265.2165 (25) 253.2161 (30) 232.9139 (10) 174.9546 (10) 164.9258 (10) 88.0387 (10) | C44H87O5N | -1.5 | 37 | | | 34_1; 36_1, 36_2; 25_1, 25_2 | Cer18:1;O3/26:0; O²,f | literature [30], LDA[4] (supplementary figure S14) |

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Supplementary table S5: ^{13}C and ^{1}H NMR-shifts of compounds **26, 27, 29** and of apigenin (pyridine-d$_5$, 700 and 175 MHz, respectively)

position	26 δ$_C$ (ppm)	26 δ$_H$ (ppm)	27 δ$_C$ (ppm)	27 δ$_H$ (ppm)	29 δ$_C$ (ppm)	29 δ$_H$ (ppm)	apigenin δ$_C$ (ppm)	apigenin δ$_H$ (ppm)
2	164.5	-	164.3	-	164.3	-	164.6	-
3	103.6	6.89 s	103.4	6.96 s	103.4	6.95 s	104.0	6.93 s
4	183.0	-	183.1	-	183.0	-	182.8	-
4a	105.0	-	104.9	-	104.8	-	105.0	-
5	162.8	-	162.7	-	162.6	-	163.2	-
6	100.7	7.04 s	100.7	7.00 s	100.9	7.01 s	100.1	6.76 br s
7	166.6	-	166.7	-	n. d.	-	165.9	-
8	101.2	-	101.0	-	101.3	-	94.9	6.84 br s
8a	n. d.	-	n.d	-	n. d.	-	158.5	-
1´	122.5	-	122.6	-	122.5	-	122.3	-
2´	128.7	7.84 d (8.5 Hz)	109.4	7.40 br s	109.4	7.37 br s	129.0	7.94 d (9.0 Hz)
3´	116.9	7.09 d (8.5 Hz)	148.8	-	148.8	-	116.9	7.23 d (9.0 Hz)
4´	162.5	-	152.2	-	152.2	-	162.7	-
5´	116.9	7.09 d (8.5 Hz)	116.8	7.13 d (8.3 Hz)	116.9	7.12 d (8.5 Hz)	116.9	7.23 d (9.0 Hz)
6´	128.7	7.84 d (8.5 Hz)	120.9	7.50 d (8.3 Hz)	121.0	7.50 d (8.5 Hz)	129.0	7.94 d (9.0 Hz)
2´´	164.5	-	164.6	-	164.3	-	-	-
3´´	103.6	6.89 s	103.4	6.90 s	103.4	6.95 s	-	-
4´´	183.0	-	183.1	-	183.0	-	-	-
4a´´	105.0	-	104.9	-	104.8	-	-	-
5´´	162.8	-	162.7	-	162.6	-	-	-
6´´	100.7	7.04 s	100.7	7.01 s	100.9	7.01 s	-	-
7´´	166.6	-	n. d.	-	n. d.	-	-	-
8´´	101.2	-	101.0	-	101.3	-	-	-
8a´´	n. d.	-	n. d.	-	n. d.	-	-	-
1´´´	122.5	-	122.6	-	122.5	-	-	-
2´´´	128.7	7.84 d (8.5 Hz)	128.6	7.83 d (8.6 Hz)	109.4	7.37 br s	-	-
3´´´	116.9	7.09 d (8.5 Hz)	116.8	7.10 d (8.6 Hz)	148.8	-	-	-
4´´´	162.5	-	162.6	-	152.2	-	-	-
5´´´	116.9	7.09 d (8.5 Hz)	116.8	7.10 d (8.6 Hz)	116.9	7.12 d (8.5 Hz)	-	-
6´´´	128.7	7.84 d (8.5 Hz)	128.6	7.83 d (8.6 Hz)	121.0	7.50 d (8.5 Hz)	-	-
3´CH$_3$	-	-	55.7	3.81 s	56.0	3.81 s	-	-
3´´´-CH$_3$	-	-	-	-	56.0	3.81 s	-	-
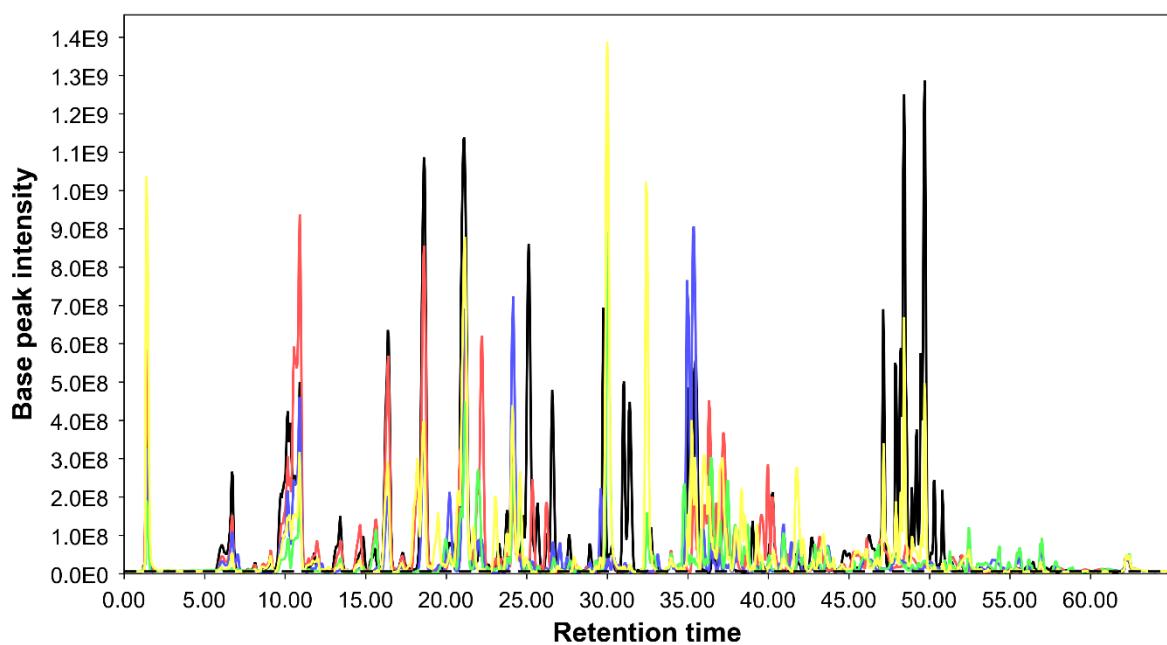
Figure S1. Superposition of HESI negative ion mode base peak chromatograms (*m/z* 133-2000) of five representative ethanolic leaf extracts from different Lonicera species. black: L3_1 (*L. hypoglauca*); red: L10_1 (*L. confusa*); blue: L32_1 (L. *acuminata*); green: L24_1 (*L. japonica*); yellow: L15_1 (*L. macrantha*). Superposition of LC-HRMS raw data was generated using MzMine 2 (doi:10.1186/1471-2105-11-395.)
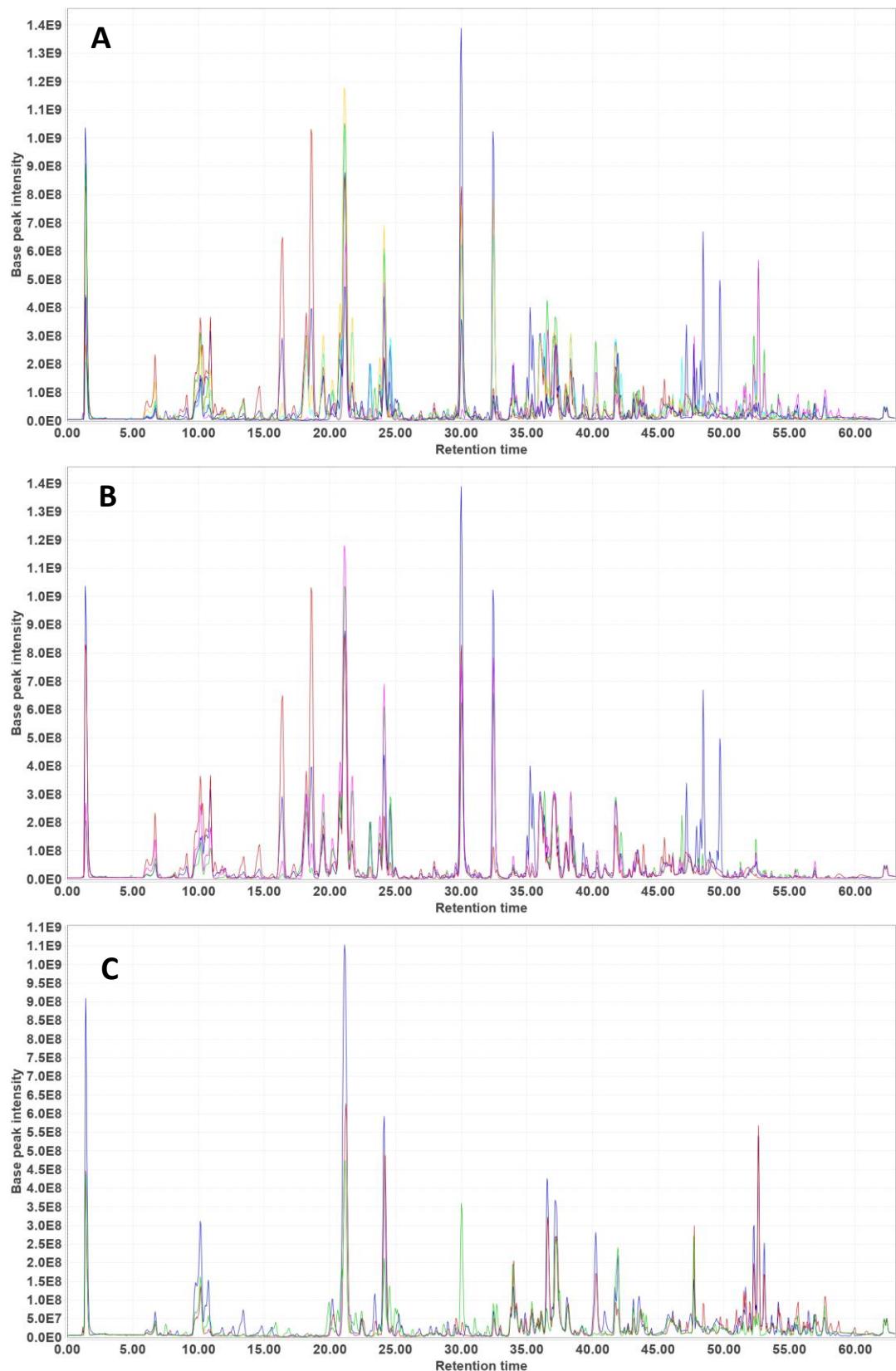
Figure S2: Superposition of UHPLC-HRMS HESI negative ion mode base peak chromatograms (*m/z* 132-2000) of **(A)** all *Lonicera macrantha* samples (L12, 15, 16, 17, 21, 31, 33), **(B)** *L. macrantha* samples of cluster 1 ([t1]/[t2] = -0.5/-0.5; samples L12, 15, 16, 17), **(C)** *L. macrantha* samples of cluster 2 (t1]/[t2] = -0.5/+0.5; samples 31, 31, 33) in PCA score scatter plot [t1]/[t2] (Figure 1). Generated with MzMine 2 (doi:10.1186/1471-2105-11-395.)

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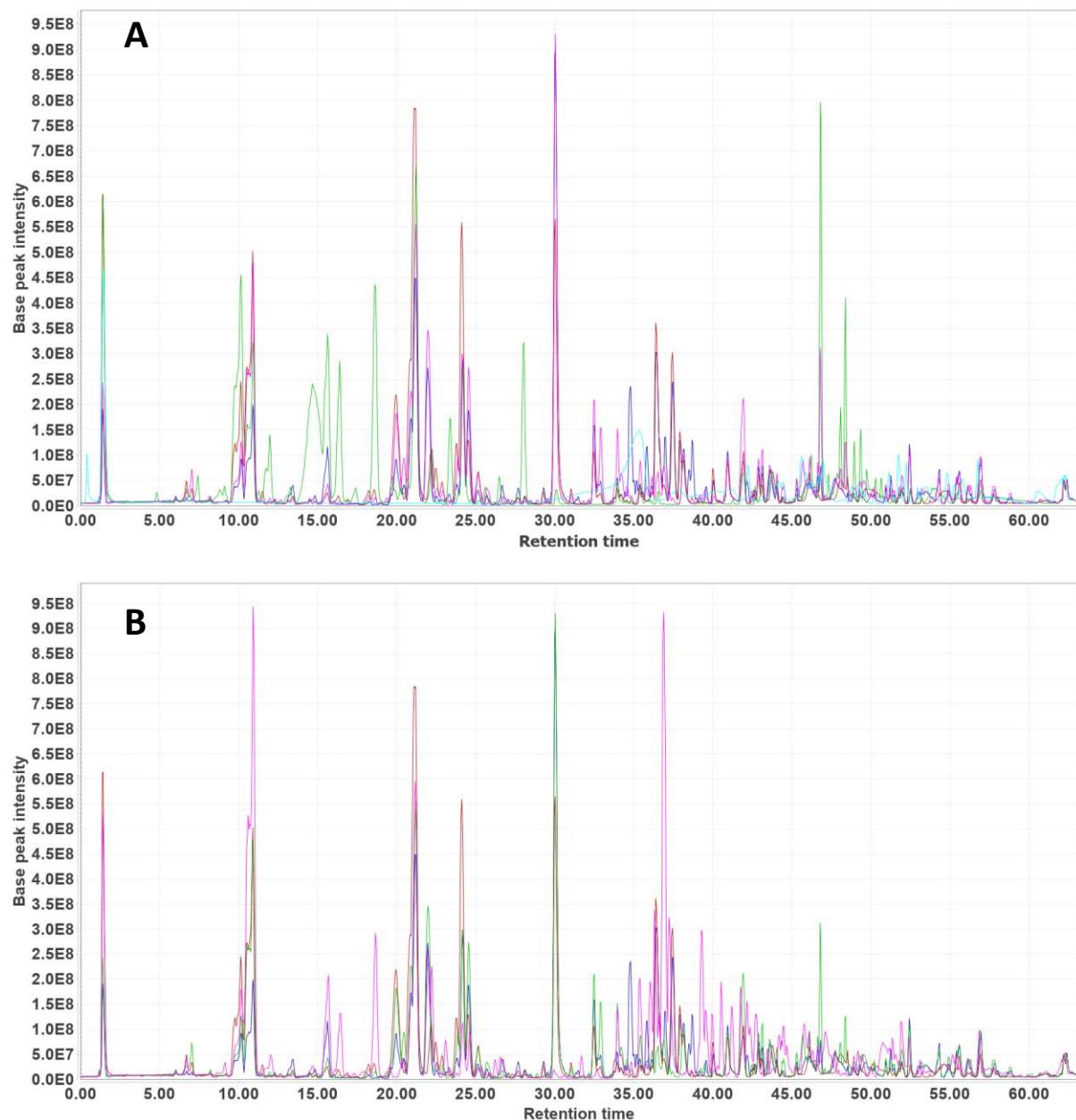
Figure S3: Superposition of UHPLC-HRMS HESI negative ion mode base peak chromatograms (*m/z* 132-2000) of **(A)** all *Lonicera japonica* samples (L23, 24, 25, 35, 36) and **(B)** *L. japonica* leaf samples only (L23, 24, 25, 36). Generated with MzMine 2 (doi:10.1186/1471-2105-11-395.)
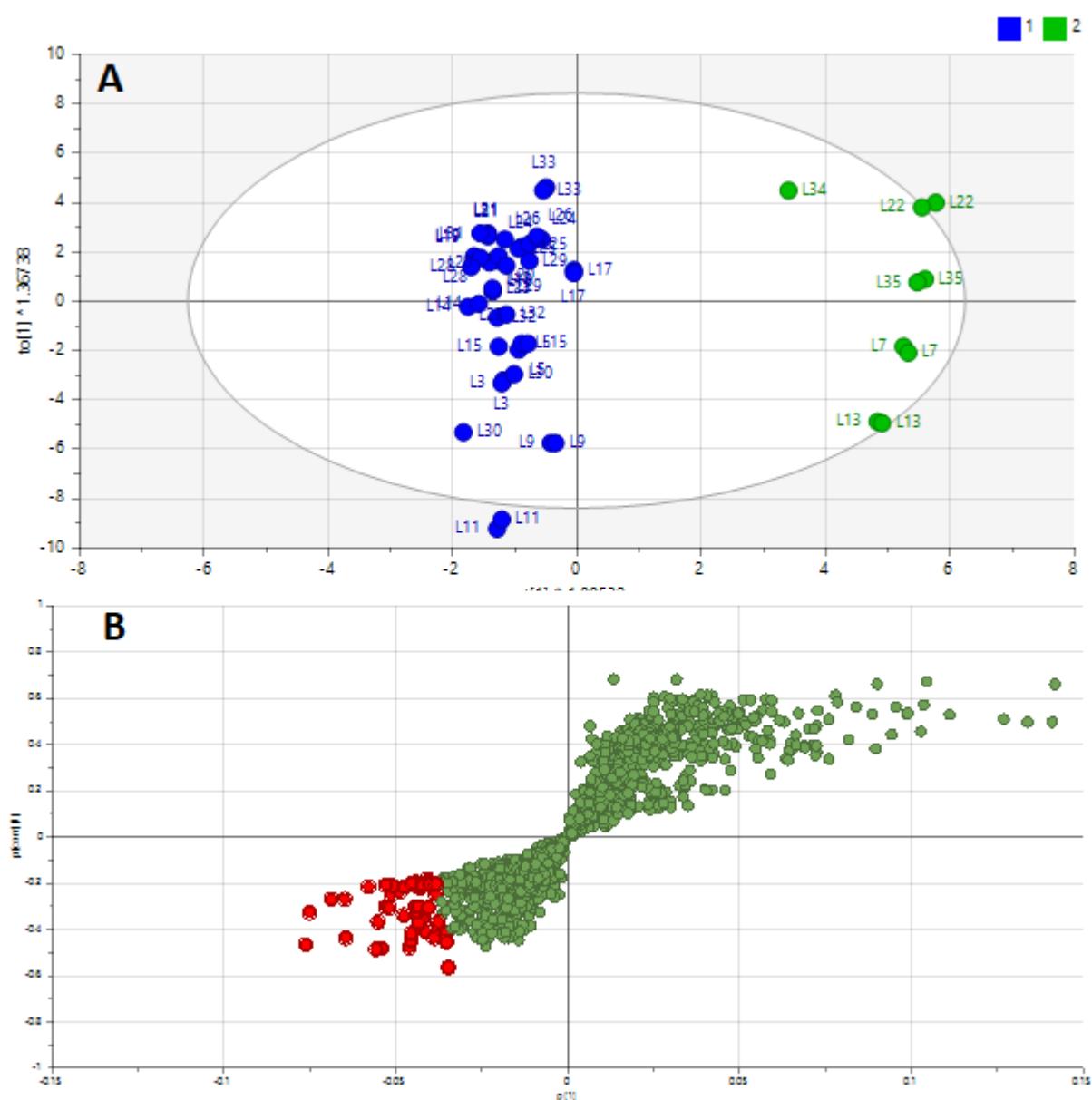
Figure S4: OPLS-DA model of CD-processed UHPLC-HRMS data in correlation with activity on transactivation of an NF-κB-driven luciferase reporter gene in TNF-α- stimulated HEK293/NF-κB-luc cells. **A:** score scatter plot; blue: highly active samples; green: samples with low activity; moderately active samples were excluded from the model. **B:** S-Plot of the OPLS-DA model. Variables most likely correlated with bioactivity are marked in red and listed in Table 2 and Supplementary Table S4.
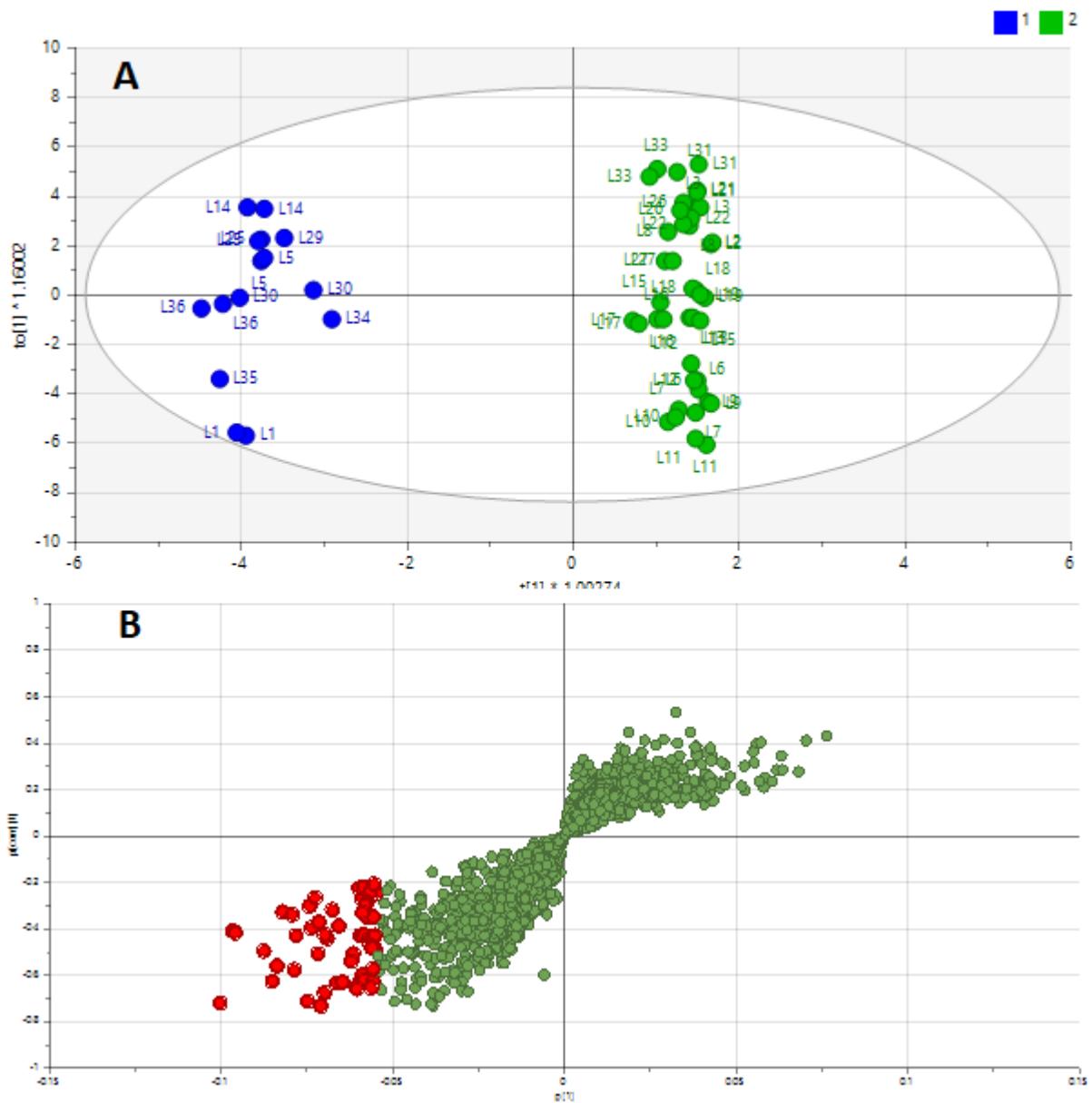
Figure S5: OPLS-DA model of CD-processed UHPLC-HRMS data in correlation with activity on IL-8 expression in LPS-stimulated HUVECtert cells. **A:** score scatter plot; blue: active samples; green: inactive samples; moderately active samples were excluded from the model. **B:** S-Plot of the OPLS-DA model. Variables most likely correlated with bioactivity are marked in red and listed in Table 2 and Supplementary Table S4.
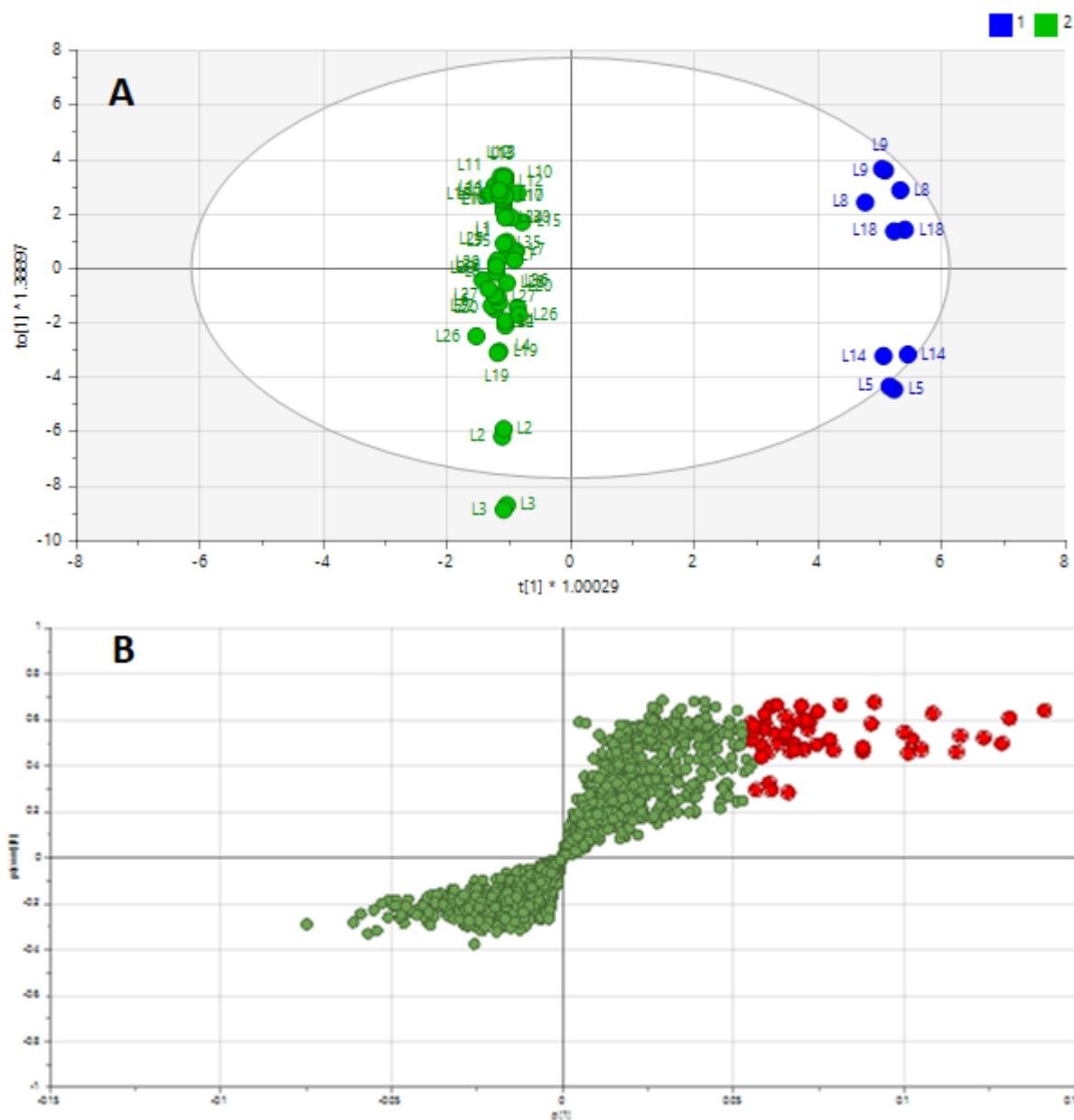
Figure S6: OPLS-DA model of CD-processed UHPLC-HRMS data in correlation with activity on NO production in LPS/IFNγ- stimulated RAW 264.7 mouse macrophages. **A:** score scatter plot; blue: active samples; green: inactive samples; moderately active samples were excluded from the model**. B**: S-Plot of the OPLS-DA model. Variables most likely correlated with bioactivity are marked in red and listed in Table 2 and Supplementary Table S4.
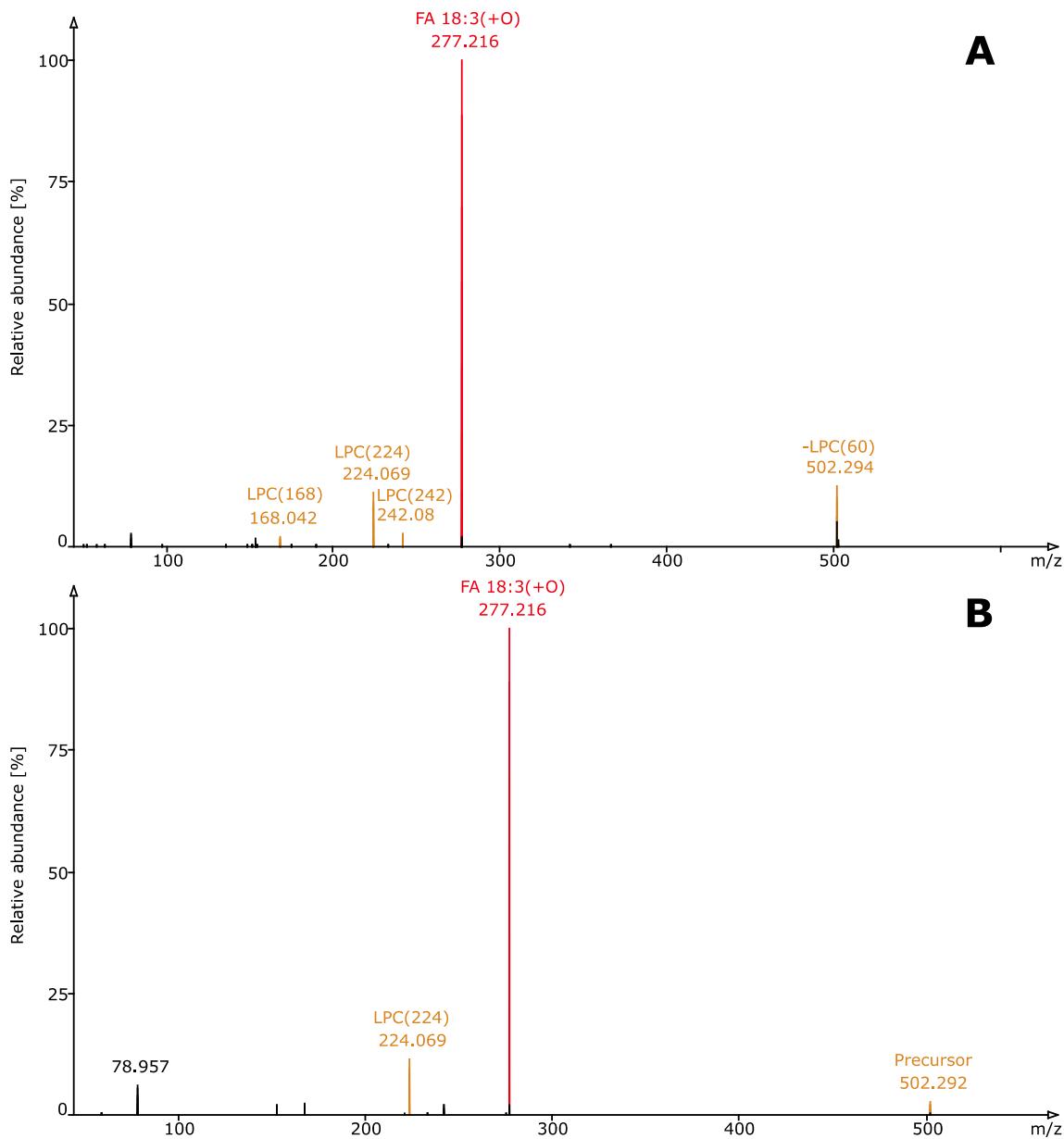
Supplementary Figure S7: MS/MS spectra of LPC 18:3 (**40**), assigned with LDA. **A**, precursor: *m/z* 562.314 [M+HCOO]⁻, retention time: 44.18 min, file: Lonicera-L25-fl-1_1; **B**, precursor *m/z* 502.290 [M-CH₃]⁻, retention time: 44.08 min; file: Lonicera-L25-fl-1_1
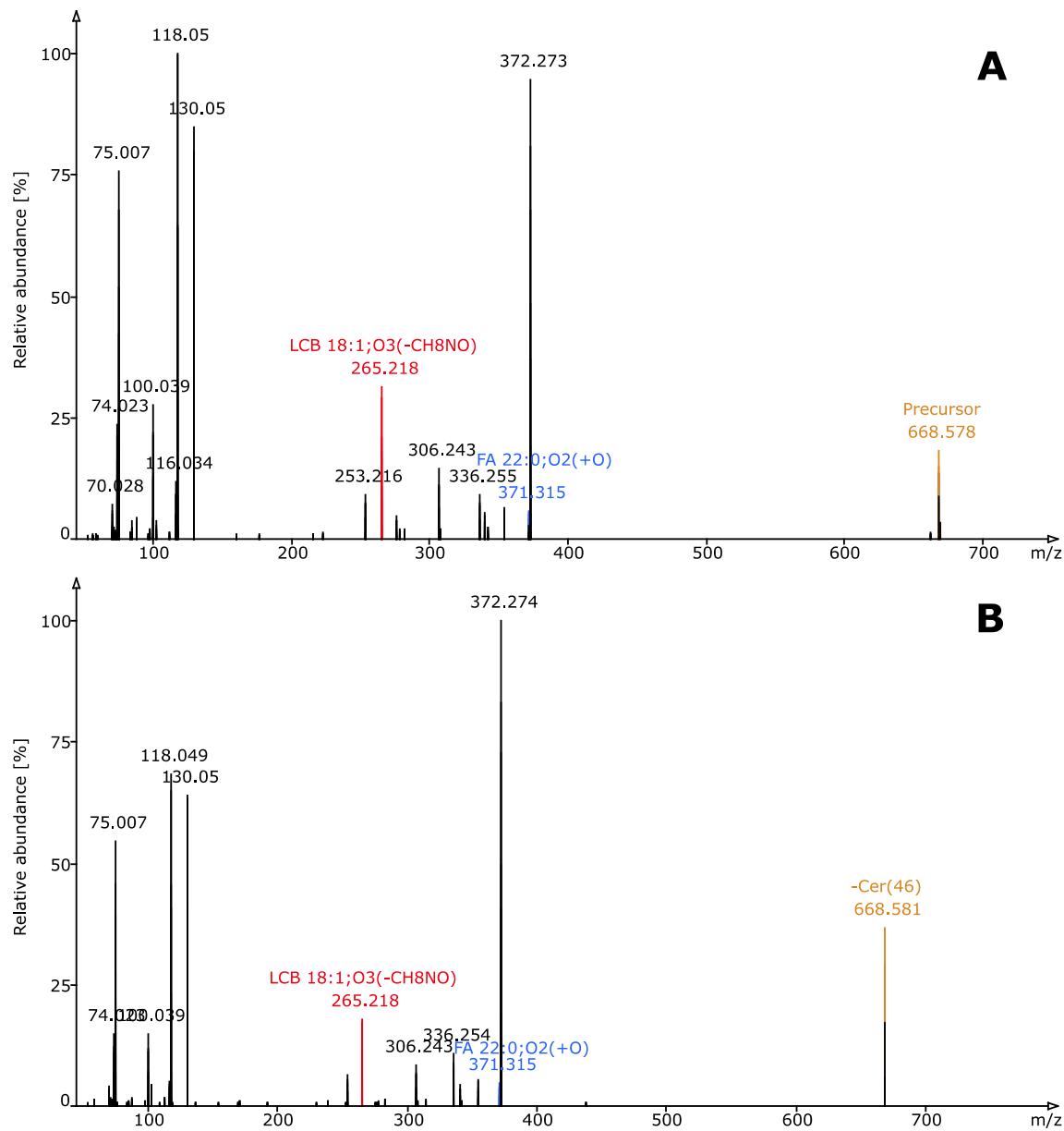
Supplementary Figure S8: MS/MS spectra of Cer 18:1;O3/22:0;O2 (**59**), assigned with LDA. **A**, precursor: *m/z* 668.580 [M-H]⁻, retention time: 54.32 min, file: Lonicera-jap-fl-1_1; **B**, precursor *m/z* 714.590 [M+HCOO]⁻, retention time: 54.27 min, file: Lonicera-jap-fl-1_1
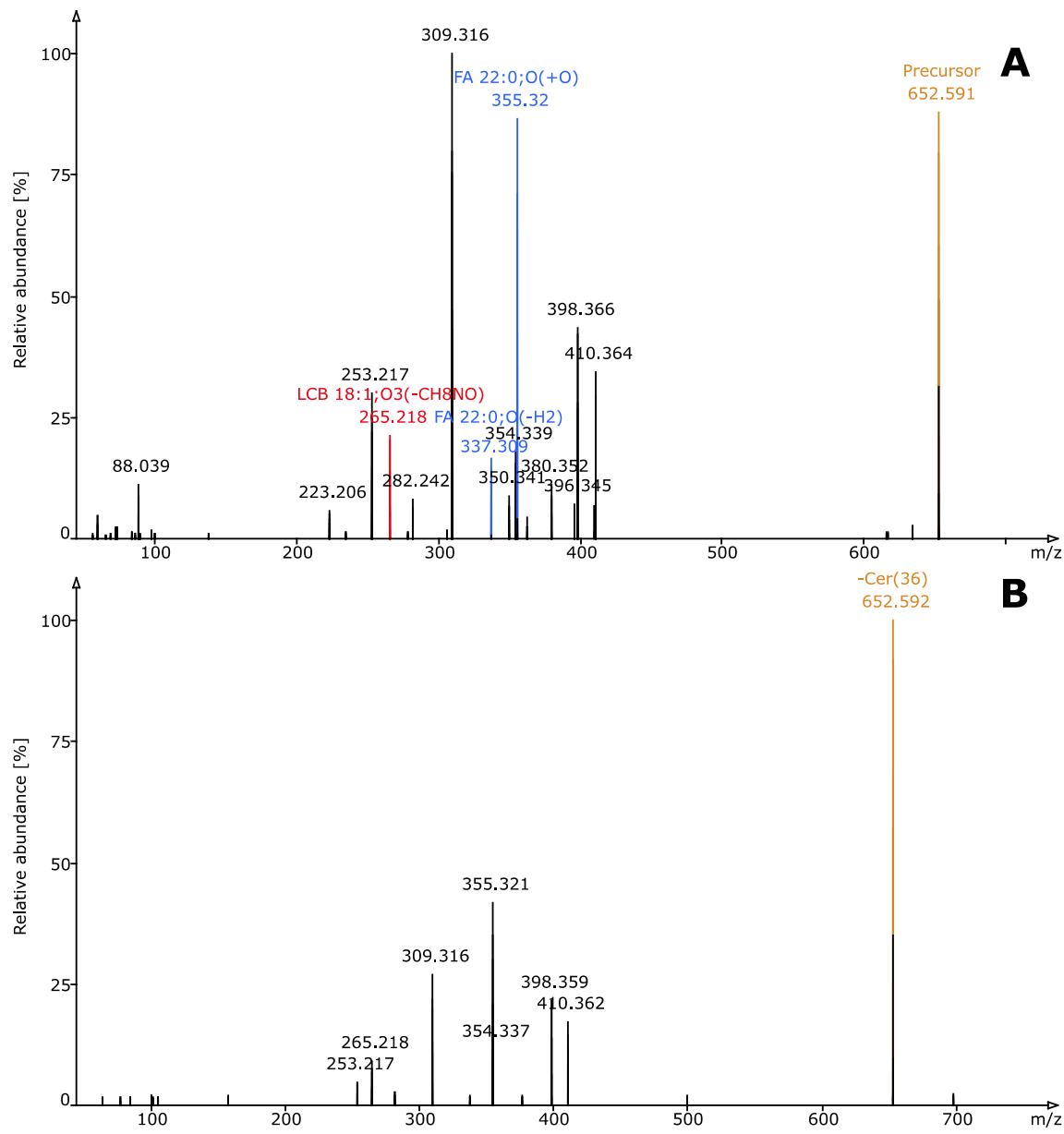
Supplementary figure S9: MS/MS spectra of Cer 18:1;O3/22:0;O (**60**), assigned with LDA. **A**, precursor: *m/z* 652.590 [M-H]⁻, retention time: 55.50 min, file: Lonicera-jap-fl-1_1; **B**, precursor *m/z* 688.560 [M+Cl]⁻, retention time: 55.49 min; file: Lonicera-jap-fl-1_1
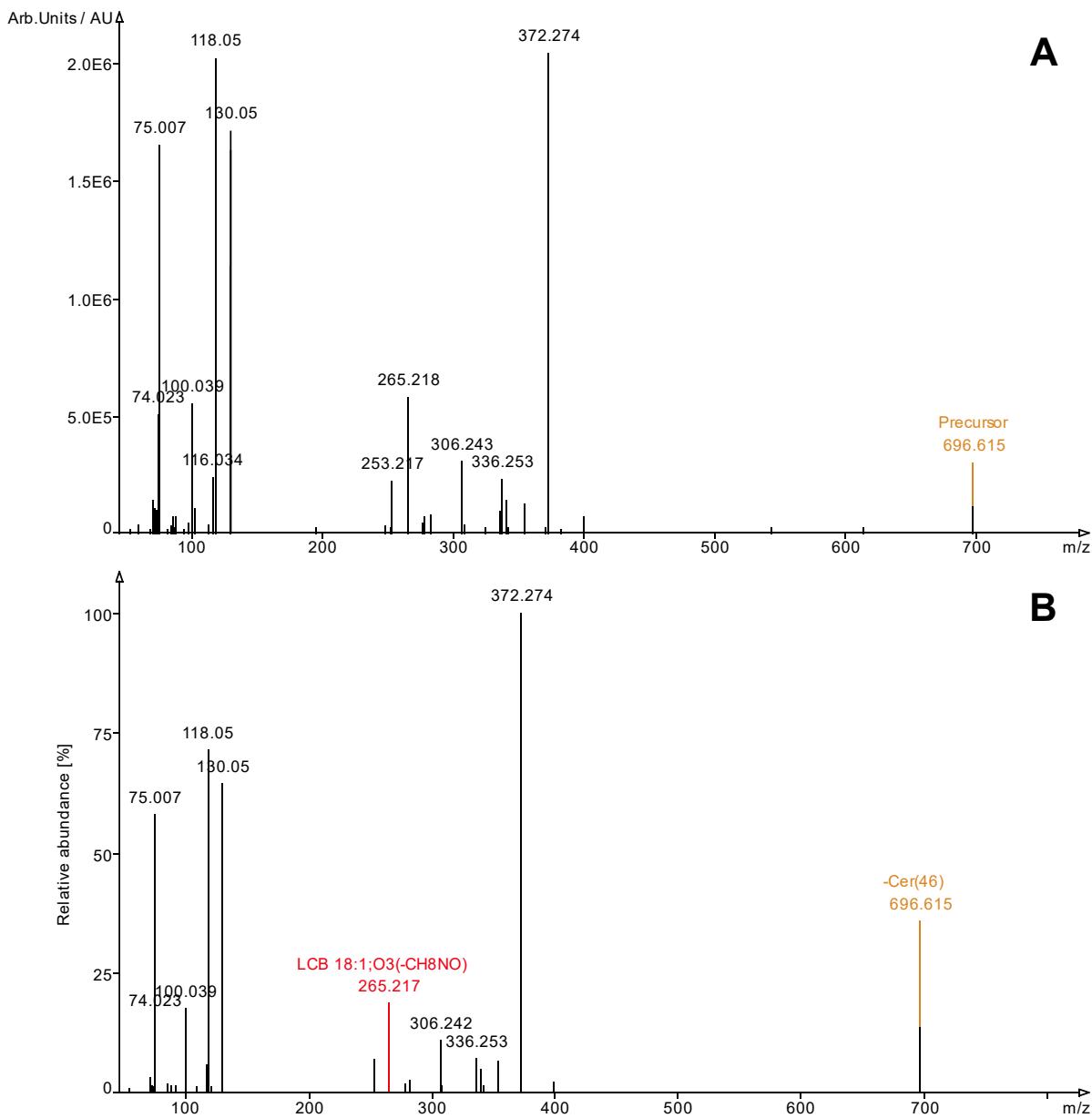
Supplementary figure S10: MS/MS spectra of Cer 18:1;O3/24:0;O2 (**61**), assigned with LDA. **A**, precursor: *m/z* 696.610 [M-H]⁻, retention time: 55.55 min, file: Lonicera-jap-fl-1_1; **B**, precursor *m/z* 742.619 [M+HCOO]⁻, retention time: 55.64 min, file: Lonicera-jap-fl-1_1
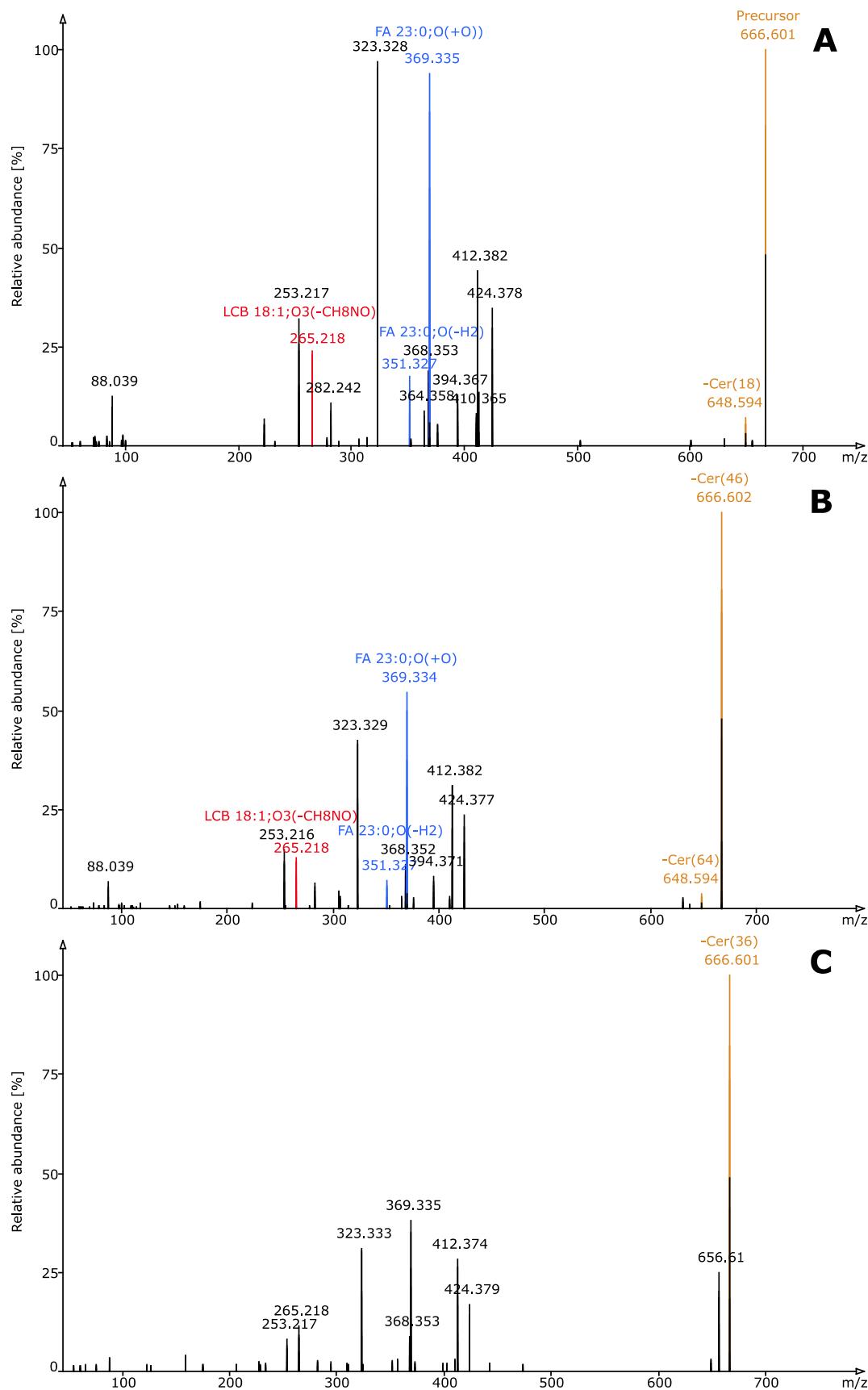
Supplementary Figure S11: MS/MS spectra of Cer 18:1;O3/23:0;O; (**62**), assigned with LDA. **A**, precursor: *m/z* 666.600 [M-H]⁻, retention time: 56.20 min, file: Lonicera-jap-fl-1_1; **B**, precursor *m/z* 712.610 [M+HCOO]⁻ , retention time: 56.18 min, file: Lonicera-jap-fl-1_1; **C**: precursor: 702.580 [M+Cl]⁻, retention time: 56.19 min, file: Lonicera-jap-fl-1_1
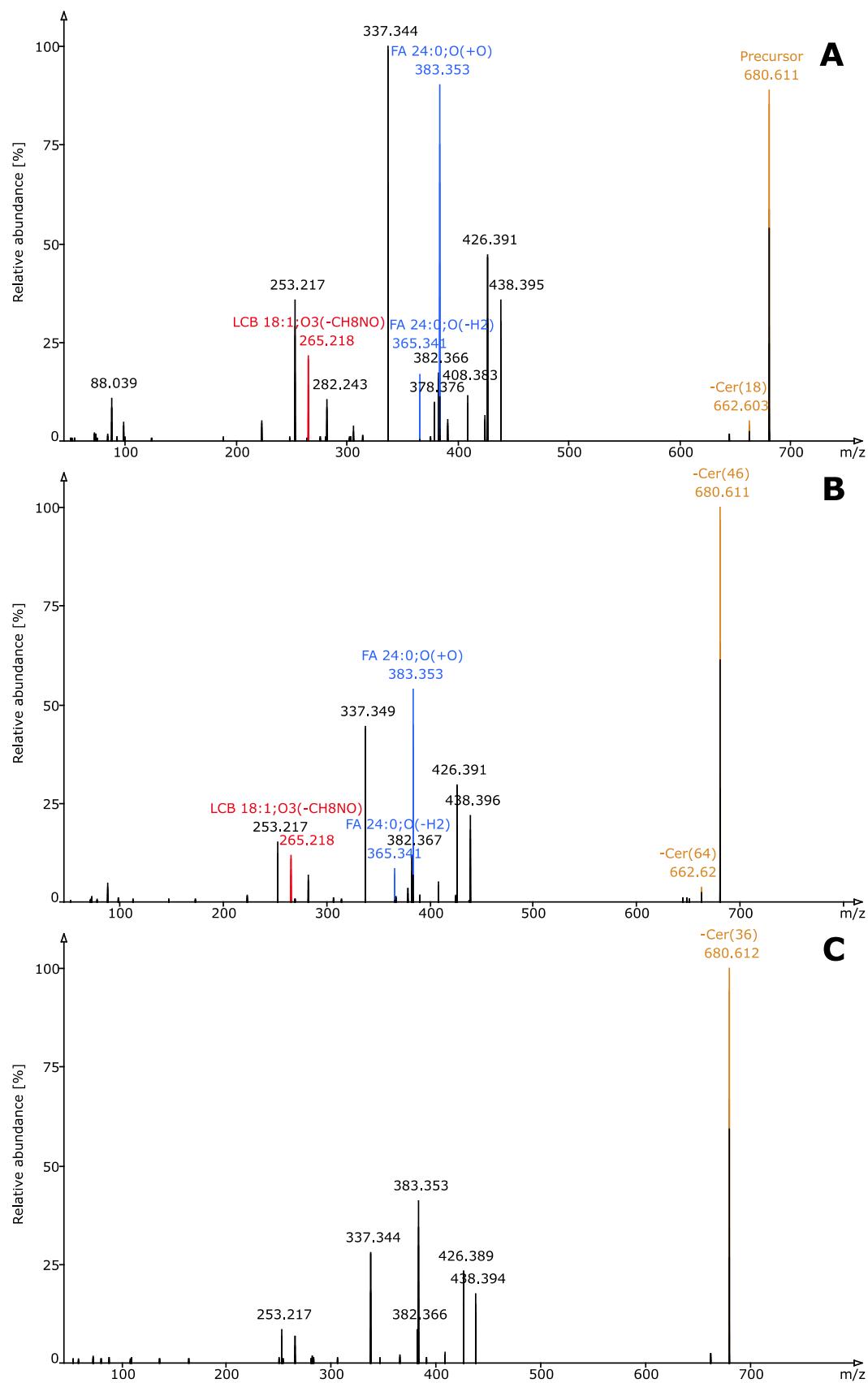
Supplementary Figure S12: MS/MS spectra of Cer 18:1;O3/24:0;O; (**63**), assigned with LDA. **A**, precursor: *m/z* 680.620 [M-H]⁻, retention time: 56.98 min; file: Lonicera-jap-fl-1_1; **B**, precursor *m/z* 726.624 [M+HCOO]⁻, retention time: 56.98 min, file: Lonicera-jap-fl-1_1; **C**: precursor: 716.598 [M+Cl]⁻, retention time: 56.92 min; file: Lonicera-jap-fl-1_1
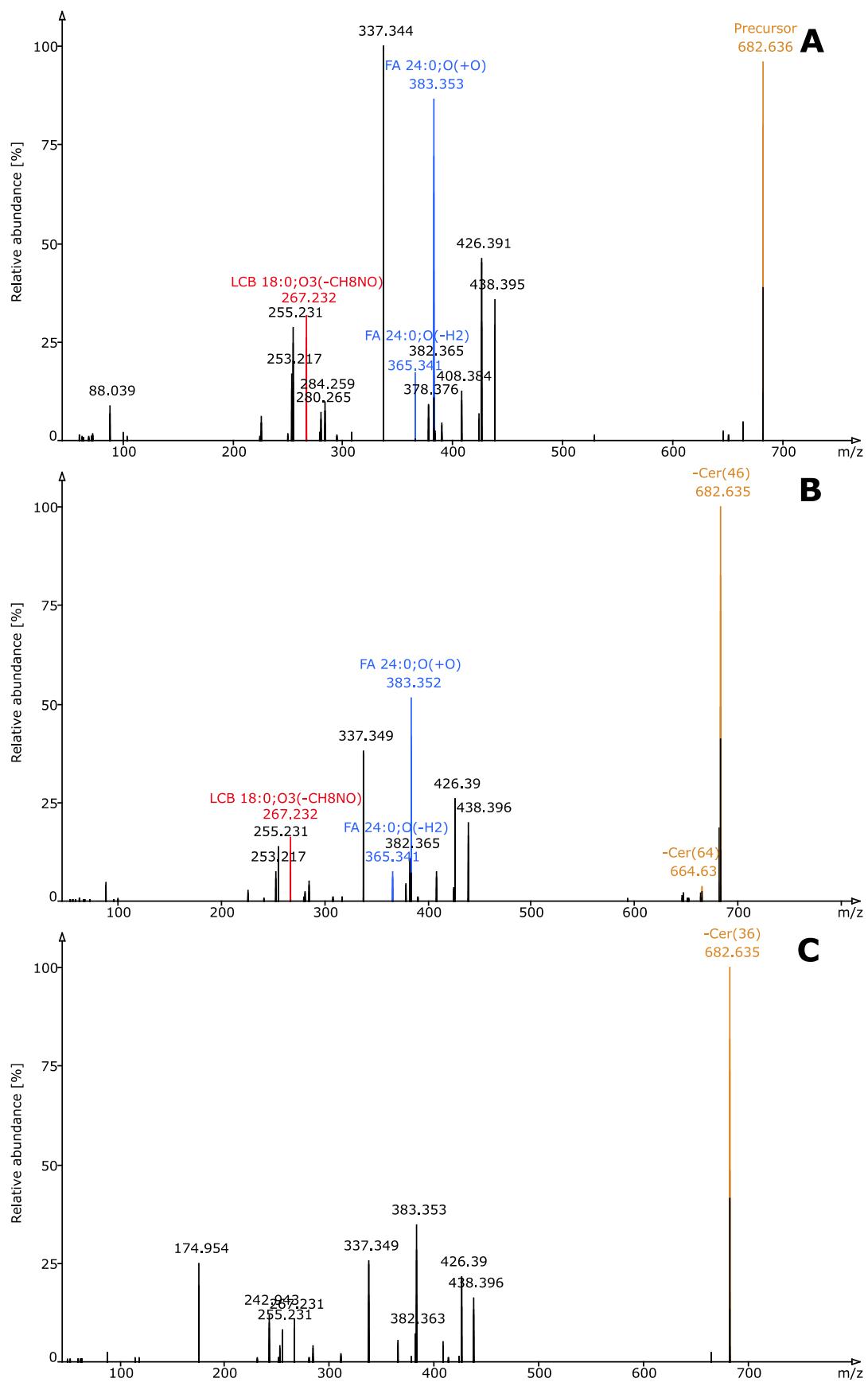
Supplementary Figure S13: MS/MS spectra of Cer 18:0;O3/24:0;O (**64**), assigned with LDA. **A**, precursor: *m/z* 682.630 [M-H]⁻, retention time: 57.95 min, file: Lonicera-jap-fl-1_1; **B**, precursor *m/z*

728.640 [M+HCOO]⁻, retention time: 57.88 min, file: Lonicera-jap-fl-1_1; **C**: precursor: *m/z* 718.610 [M+Cl]⁻, retention time: 57.73 min; file: Lonicera-jap-fl-1_1
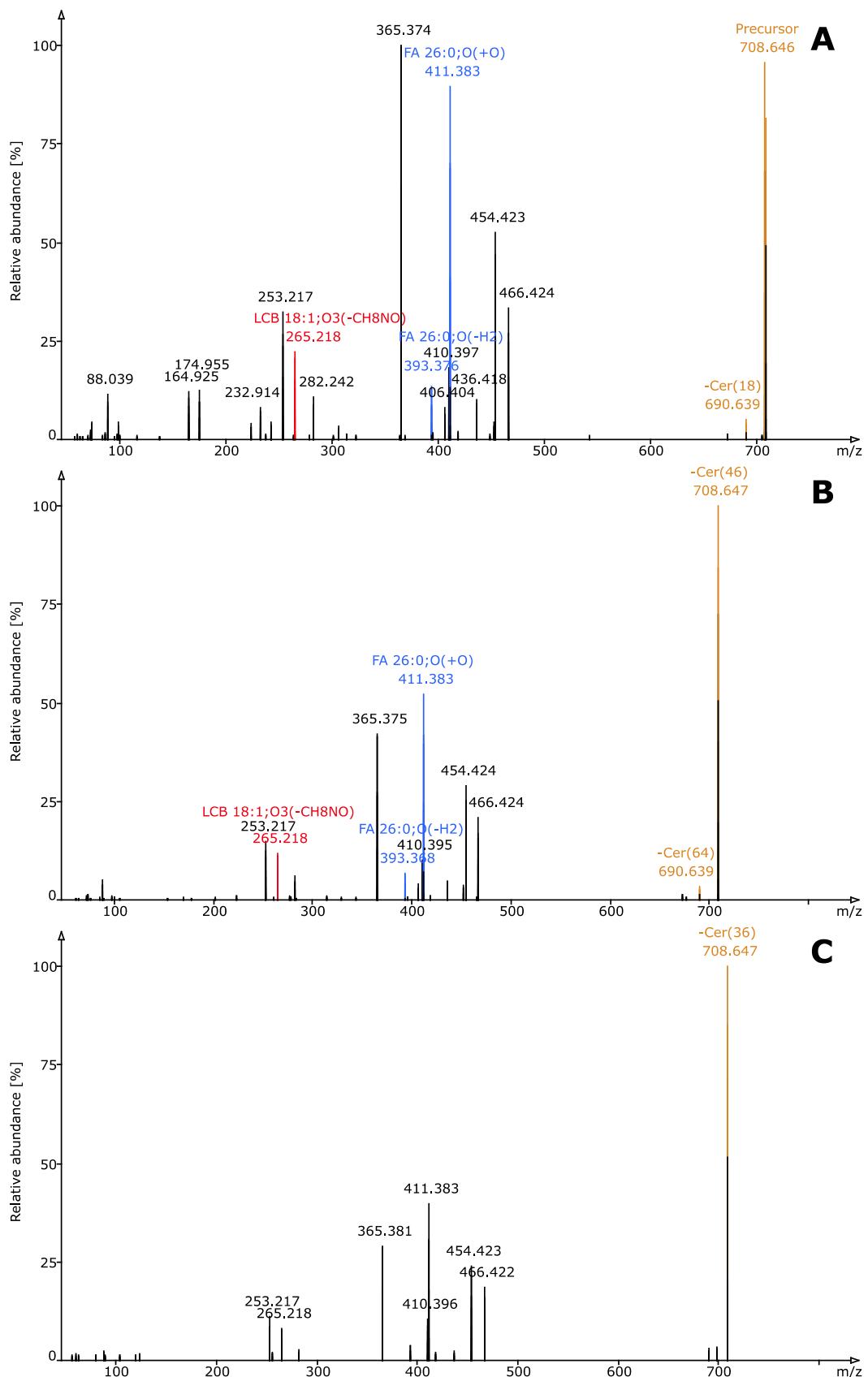
Supplementary Figure S14: MS/MS spectra of Cer 18:1;O3/26:0;O (**65**), assigned with LDA. **A**, precursor: *m/z* 708.650 [M-H]⁻, retention time: 58.88; file: Lonicera-jap-fl-1_1; **B**, precursor *m/z* 754.650

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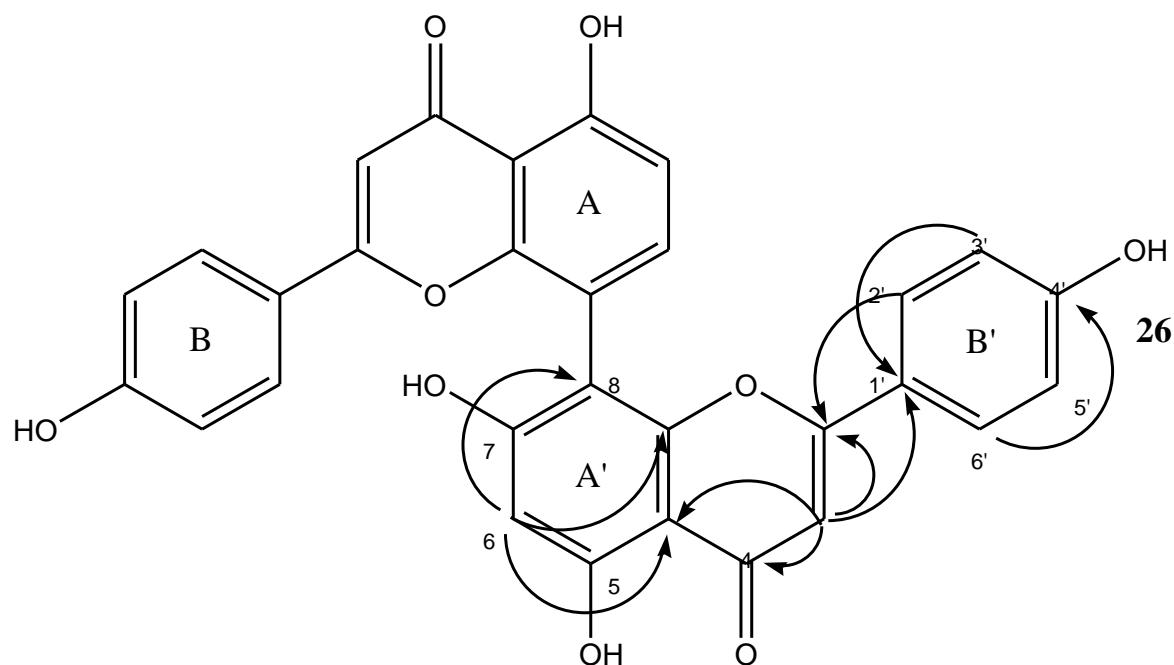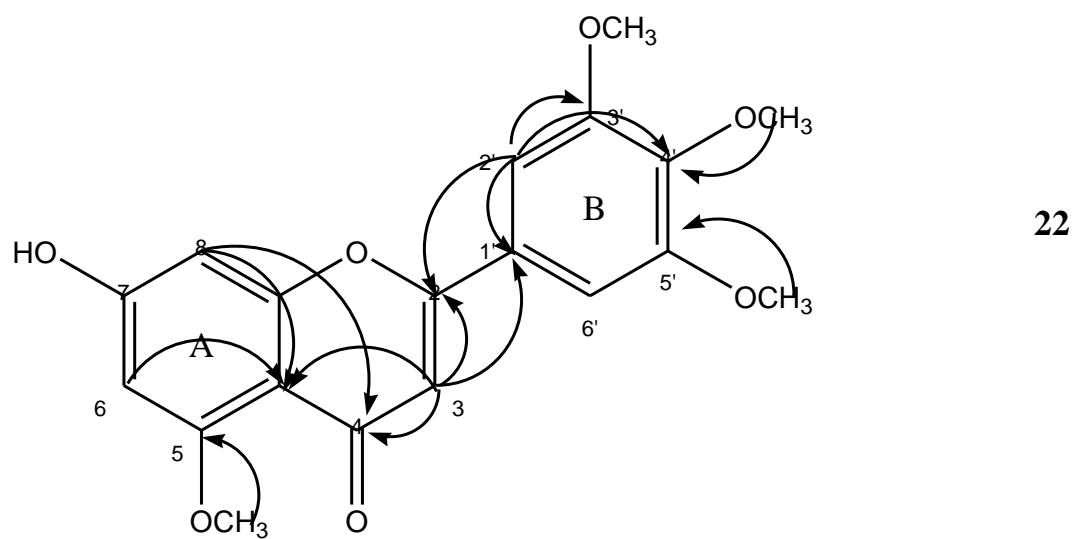
Figure S15: HMBC correlations observed for compounds 22 and 26
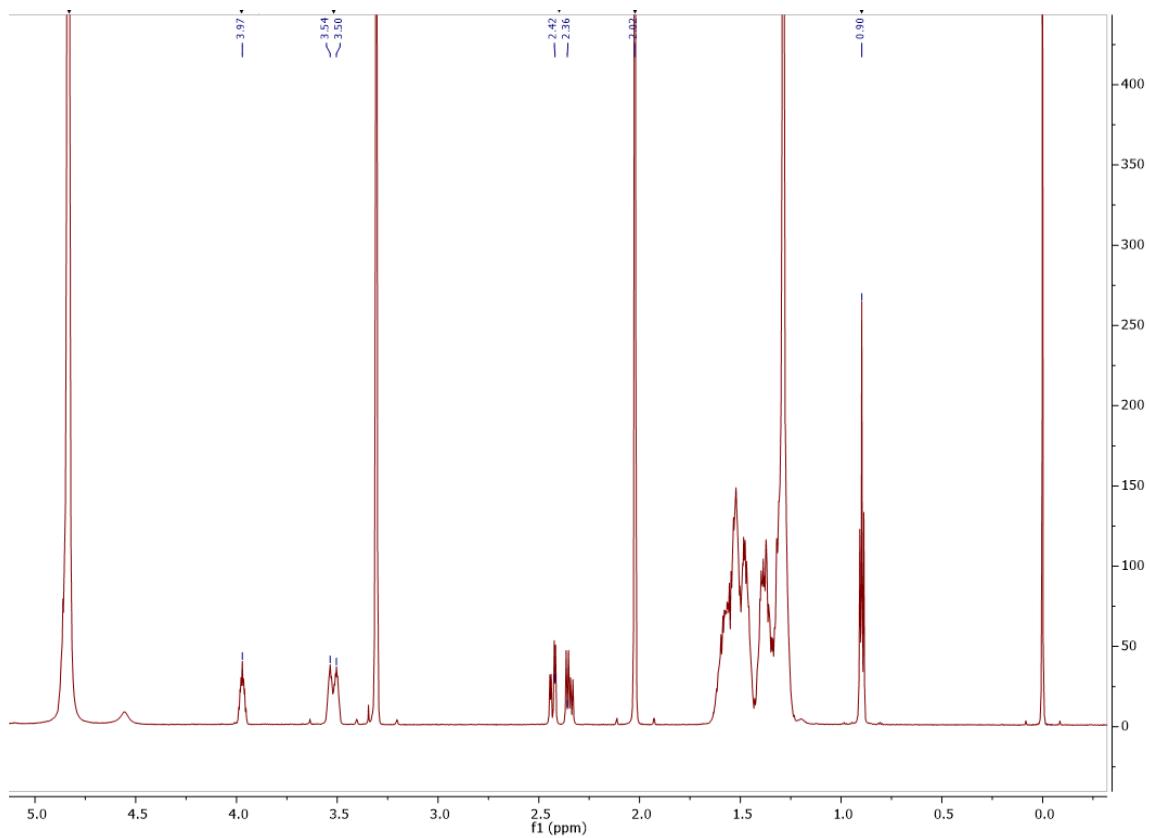
Supplementary figure S16: ^{1}H NMR spectrum of compound **46** in MeOH-d$_4$ (700 MHz, TMS, 298 K)
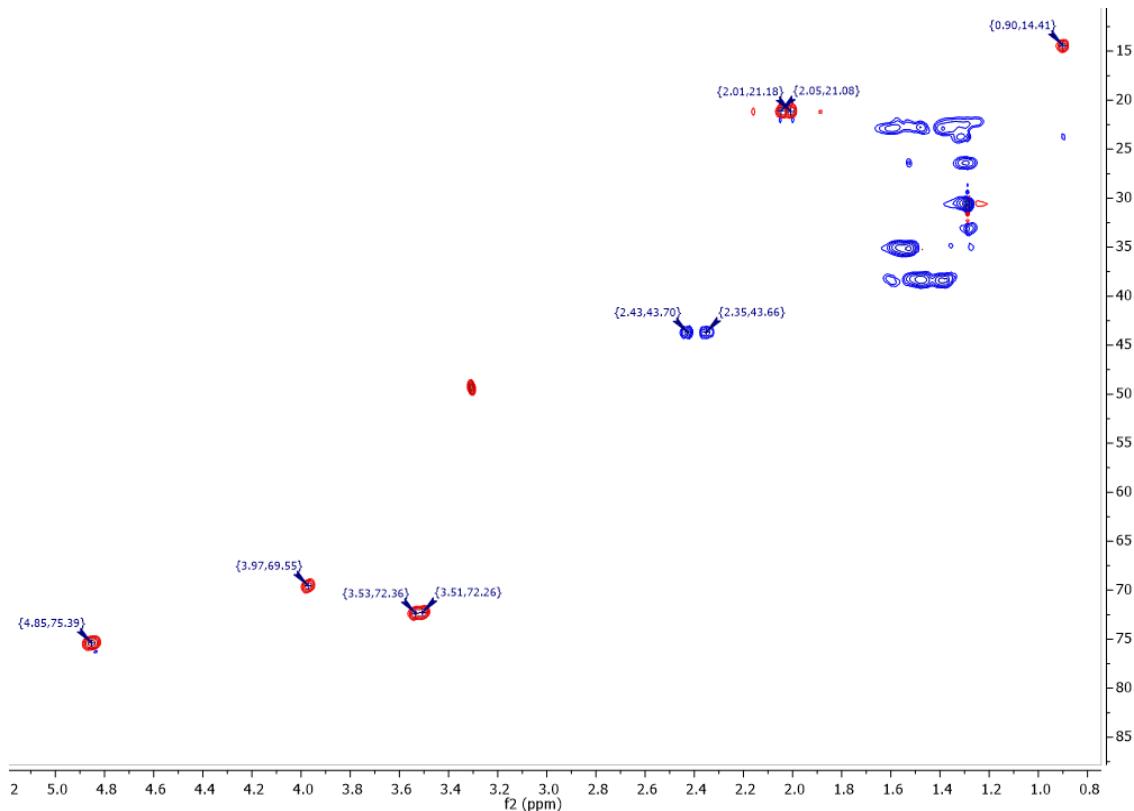

**Supplementary figure S17:** HSQC spectrum of compound **46** in MeOH-d$_4$ (TMS, 298 K)
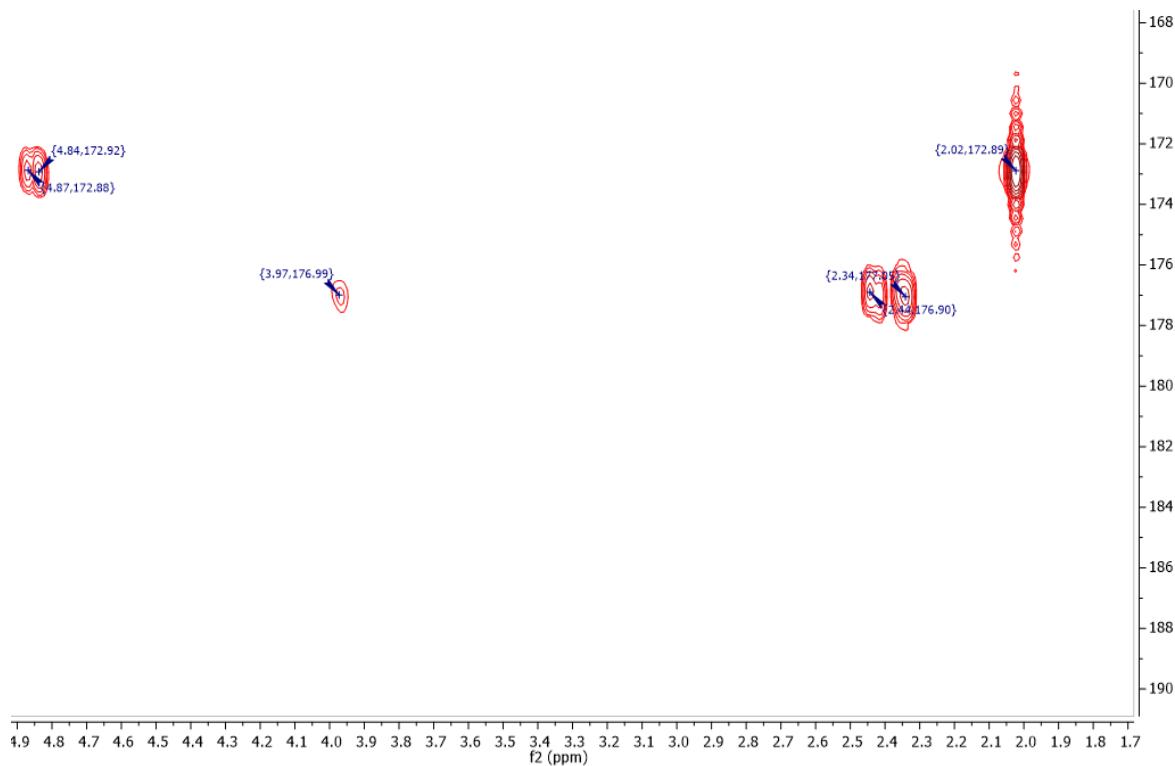
Supplementary figure S18: Correlations to carbonyl functions in the HMBC spectrum of compound **46** in MeOH-d$_4$ (TMS, 298 K)
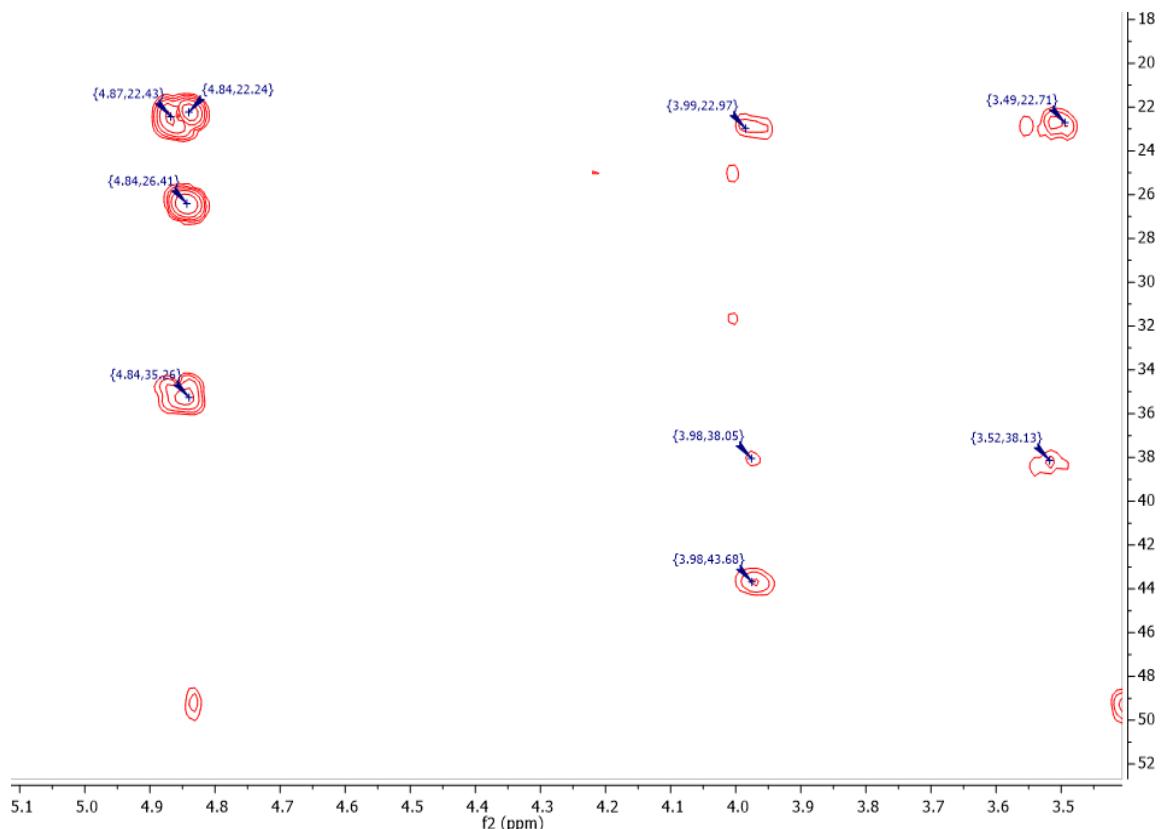

Supplementary figure S19: Non-carbonyl HMBC correlations of CHOH and CHOCOCH$_3$ groups in the HMBC spectrum of compound **46** in MeOH-d$_4$ (TMS, 298 K)
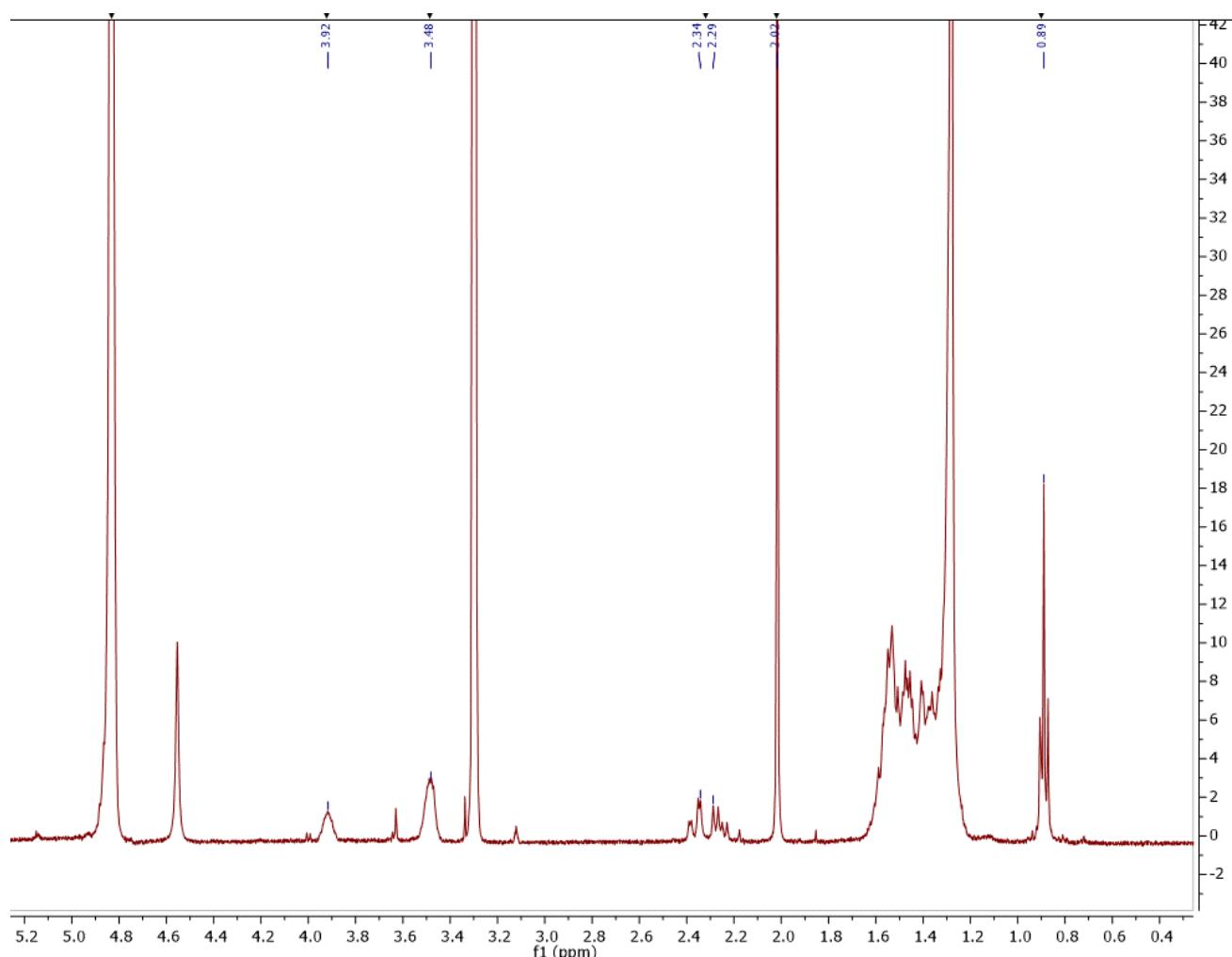
Supplementary figure S20: ^{1}H NMR spectrum of compound **43** in MeOH-d$_4$ (700 MHz, TMS, 298 K)
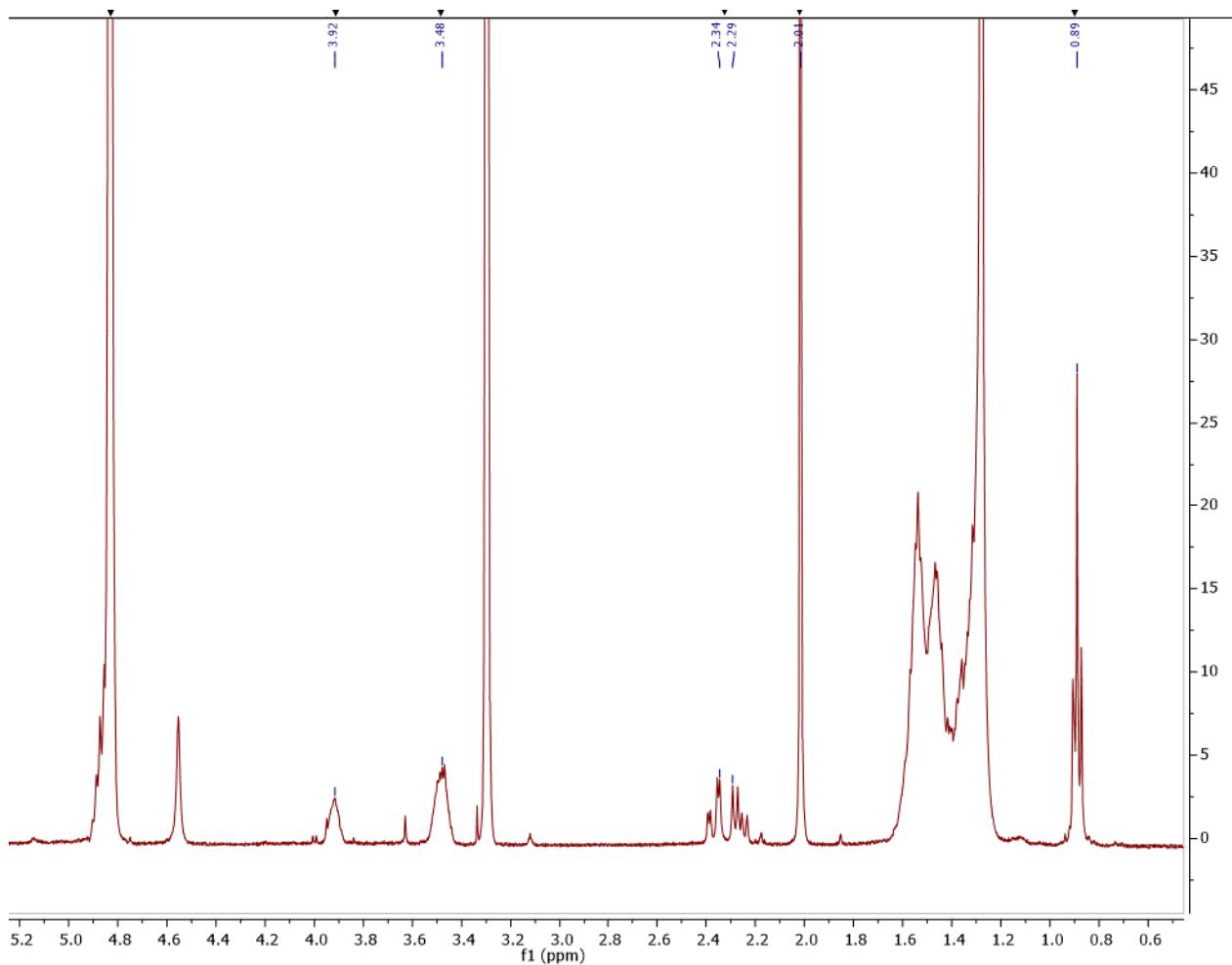
Supplementary figure S21: ^{1}H NMR spectrum of compound **44** in MeOH-d4 (700 MHz, TMS, 298 K)
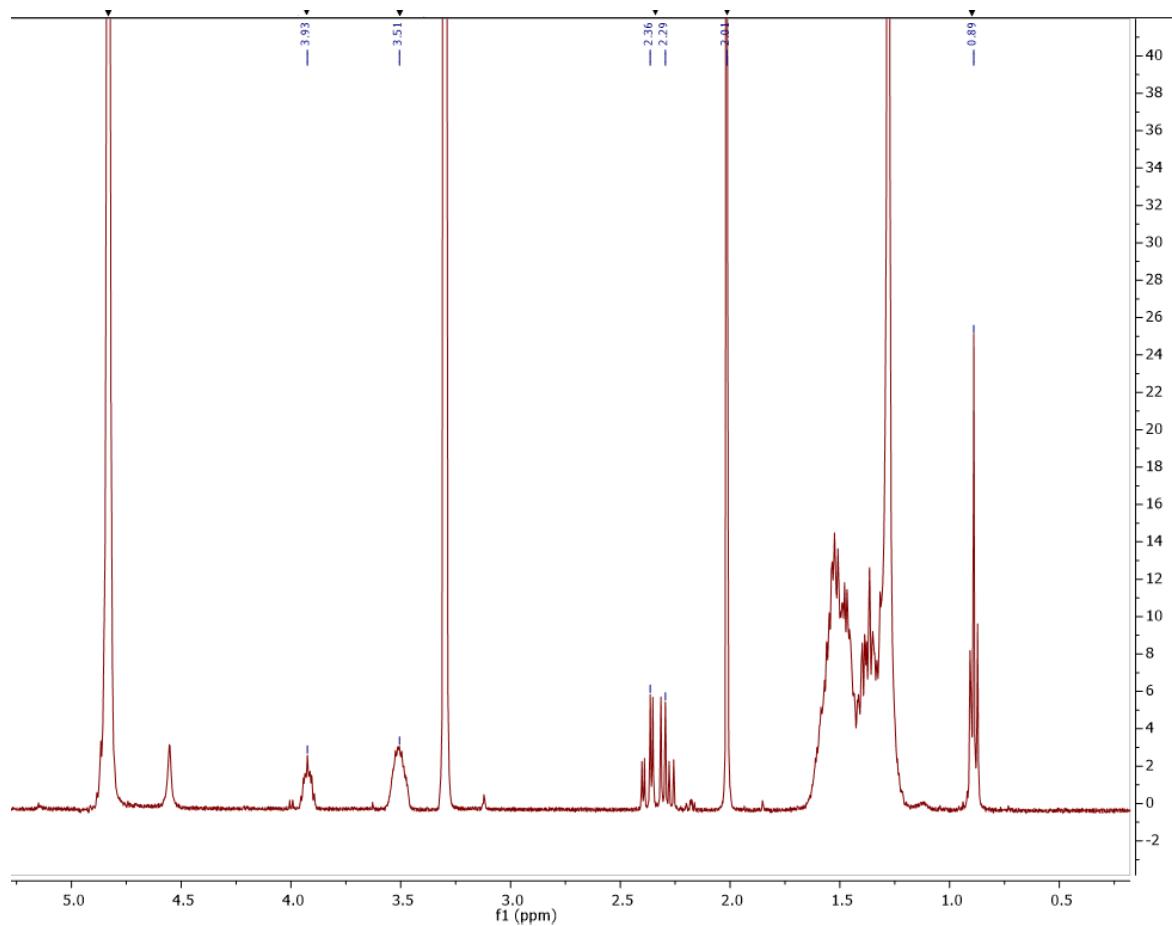
Supplementary figure S22: ^1H NMR spectrum of compound **54** in MeOH-d_4 (700 MHz, TMS, 298 K)