

Table S1. Percentages of explained variances, eigenvalues and contribution of metabolites on the first six components of PCA

	PC1	PC2	PC3	PC4	PC5	PC6
Percentages of explained variances (%)	35.34	18.36	09.20	07.57	06.51	05.99
Eigenvalues	33.57	17.44	8.74	7.19	6.19	5.69
C1	1,692	0,385	1,350	1,405	0,003	1,166
C2	1,979	0,509	0,120	0,587	0,101	1,164
C3	0,488	2,214	2,385	1,805	1,204	0,450
C4	0,000	0,691	2,960	2,810	3,147*	0,851
C5	1,938	1,202	0,054	0,980	0,000	0,118
C6	0,121	1,116	2,810	0,768	1,308	2,012
C7	1,181	0,972	1,875	1,487	0,008	1,268
C8	2,449*	0,290	0,008	0,165	0,001	0,337
C9	2,142*	0,003	0,476	0,220	2,753	0,002
C10	2,018*	0,172	1,256	0,065	0,224	2,026
C11	0,976	0,017	1,765	0,054	1,131	6,291*
C12	2,077*	0,373	0,208	2,137	0,020	0,175
C13	2,436*	0,278	0,008	0,107	0,001	0,260
C14	0,100	0,481	1,080	0,000	0,152	6,746*
C15	2,713*	0,000	0,346	0,016	0,004	0,001
C16	0,501	0,006	0,991	1,487	3,088*	1,250
C17	1,978	1,033	0,056	0,011	0,424	0,421
C18	0,007	0,258	2,070	0,000	2,358	8,445*
C19	1,361	0,145	0,022	0,374	0,137	1,936
C20	0,533	2,020	0,082	0,087	4,414*	0,982
C21	0,418	0,066	0,288	0,291	1,736	0,697
C22	0,059	0,270	2,694	0,031	1,664	7,865*
C23	0,935	0,837	0,043	0,166	3,077*	4,430*
C24	1,536	0,712	0,420	0,585	0,347	0,017
C24a	0,430	2,553	0,159	0,949	0,593	2,427
C25	1,976	0,469	0,278	2,340	0,013	0,187
C26	0,164	0,046	0,141	2,641	0,253	0,308
C27	1,104	0,126	1,217	4,615*	0,737	0,096
C28	2,116*	0,349	0,112	2,154	0,004	0,101

C29	0,128	2,750	2,436	0,776	0,431	1,758
C30	1,154	0,108	1,826	0,029	0,756	5,477*
C31	0,592	0,328	1,746	1,832	0,440	0,113
C32	2,197*	0,030	0,258	0,652	1,233	0,096
C33	1,450	1,979	0,021	1,504	0,011	0,046
C34	2,173*	0,311	0,050	2,453	0,038	0,001
C35	0,780	0,995	1,071	3,148*	0,264	0,212
C36	1,636	1,351	0,395	0,309	0,002	0,117
C37	2,356*	0,520	0,152	1,217	0,001	0,005
C38	2,269*	0,115	0,071	1,016	0,574	0,061
C39	1,300	0,046	0,274	0,174	0,807	7,088*
C40	0,451	2,422	0,014	1,101	1,953	0,848
C41	2,027*	0,181	0,258	1,816	0,204	0,188
C42	1,590	0,030	0,085	1,737	1,477	0,934
C43	1,709	0,530	0,022	1,403	2,198	0,136
C44	2,225*	0,042	0,274	0,711	0,940	0,113
C45	0,263	0,000	5,301*	1,071	0,004	0,334
C46	1,443	0,172	0,310	1,439	0,659	0,021
C47	1,664	1,063	0,731	0,246	1,779	0,643
C48	2,080*	0,324	0,297	2,124	0,021	0,186
C49	1,551	1,675	0,125	1,160	0,033	0,086
C50	0,582	0,863	0,414	0,787	0,894	0,000
C51	1,227	1,423	0,185	3,565*	0,000	0,225
C52	1,228	0,063	2,604	0,937	0,166	2,932
C53	2,163*	0,715	1,173	0,161	0,453	0,015
C54	1,232	0,063	2,599	0,927	0,169	2,919
C55	2,566*	0,095	0,260	0,944	0,005	0,016
C56	1,115	1,591	0,098	3,509*	0,004	0,496
C57	0,835	2,026	0,580	1,003	0,231	0,389
C58	0,050	0,285	1,739	1,241	0,200	0,730
C59	0,805	0,000	0,891	0,517	5,450*	0,912
C60	1,368	0,284	2,185	0,028	0,192	2,268
C61	0,482	0,225	1,216	0,689	3,934*	0,143
C62	1,403	0,436	0,291	0,999	1,492	0,346
C63	1,177	0,207	0,454	1,693	0,632	1,063
C64	0,888	1,066	0,398	0,128	0,026	0,763

C65	1,315	0,584	0,011	0,051	1,485	0,019
C66	1,431	0,126	1,573	1,459	2,667	0,772
C67	2,398*	0,161	0,079	0,685	0,500	0,137
C68	0,482	0,225	1,216	0,689	3,934*	0,143
C69	2,258*	0,019	0,248	0,251	2,399	0,061
C70	1,154	0,000	2,850	0,137	0,817	0,657
C71	0,427	3,487*	0,354	0,522	0,316	0,142
C72	0,487	3,525*	0,120	1,122	1,118	0,105
C73	0,074	3,567*	1,200	2,115	0,246	0,319
C74	0,018	3,924*	0,231	1,375	0,449	0,072
C75	0,000	1,146	0,463	1,782	6,604*	1,032
C76	0,505	0,816	5,034*	0,990	0,038	0,266
C77	0,138	4,539*	0,205	1,380	0,025	0,073
C78	0,138	4,539*	0,205	1,380	0,025	0,073
C79	0,010	4,055*	0,000	0,272	0,200	0,513
C80	0,092	2,289	2,427	0,010	0,643	0,280
C81	0,051	5,382*	0,282	0,128	0,009	0,000
C82	0,148	3,881*	0,544	1,035	0,271	0,135
C83	0,132	2,348	0,637	0,966	1,521	3,334*
C84	0,580	2,398	0,450	0,308	0,990	0,640
C85	0,406	0,094	6,499*	2,050	0,675	0,280
C86	0,156	2,002	0,087	0,125	2,638	2,649
C87	0,006	1,275	7,142*	0,642	0,553	0,059
C88	0,269	0,701	0,863	0,072	0,006	0,600
C89	0,064	2,451	0,406	3,814*	1,833	0,305
C90	0,007	0,849	7,117*	0,058	0,028	0,543
C91	0,046	1,759	1,572	0,065	5,204*	2,311
C92	0,962	0,051	1,133	1,239	4,161*	0,081
C93	1,337	0,997	0,502	1,829	2,056	0,334
C94	1,321	0,898	0,472	2,065	2,009	0,356

Table S2. Percentages of explained variances, eigenvalues and contribution of biological activities on the first three components of PCA

		<b>PC1</b>	<b>PC2</b>	<b>PC2</b>
Percentages of explained variances (%)		<b>63.14</b>	<b>15.12</b>	<b>10.25</b>
Eigenvalue		<b>6.94</b>	<b>1.66</b>	<b>1.12</b>
Biological activities	<b>DPPH</b>	11,588*	6,255	1,772
	<b>ABTS</b>	12,548*	6,207	0,289
	<b>CUPRAC</b>	11,543*	8,557	2,165
	<b>FRAP</b>	11,989*	7,330	2,554
	<b>MCA</b>	0,019	28,044*	30,267*
	<b>PBD</b>	2,771	0,172	56,958*
	<b>AChE</b>	8,604	17,109*	4,327
	<b>BChE</b>	12,371*	0,039	0,533
	<b>Tyrosinase</b>	5,814	17,364*	0,975
	<b>Amylase</b>	12,531*	2,574	0,130
	<b>Glucosidase</b>	10,221*	6,350	0,028

\*Biological activities having highest contribution scores on principal components



1 Table S3. Upregulated and downregulated mRNA by the six sesquiterpene lactones and some phenolic compounds

	Artabsin	Dehydroleucodien	Dihydrosantamarin	Leucodin	Matricin	Tanaparthin peroxide	Neochlorogenic	Chlorogenic acid	Homoorientin	Vitexin	Isovitexin
Upregulated mRNA	BRMS1 SFRP1 MAP7 CYP3A4 HOXA11 APBP2 CASP2 ALDOA GNMT PFKFB2 SH3BGRL TRIM13 NUCB2 FOXO4 SCGB1D2 DNAJB14 GAL PPP1CB CHEK1 FADS1 TACC1 CACNG4 CHRNE CISH EPB41L3 PLK3 P2RY14 MYT1 KCNH2 PLLP SLC25A4 ZYX SFTPB NRTN WISP2 ENC1 MT1L WT1 HMGCR COL22A1 KLK13 ITGA6	PPP1CB DNAJB14 FOXO1 CACNG4 CHRNE PFKFB2 SH3BGRL TRIM13 COL22A1 KLK13 CNN2 DYSF FAM110C MYO5B PPFIBP2 LGALS9 GAL PLLP SLC25A4 ZYX TMEM56 FOXO4 CREB3L1 RNASEL PDZD2 IL4R KLK7 PLXNA2 SERPINB8 ABAT ERMP1 MSX2 EPB41L3 TRIOBP WT1 SQLE ITGAM CD68 NUCB2 NUDT11 FAM49A SLC4A11 SLC45A2 GNMT C8ORF4 FOXC1	MYT1 PFKFB2 SH3BGRL TRIM13 CACNG4 CHRNE SH3BGRL TRIM13 DNAJB14 CREB3L1 RNASEL KCNH2 PLLP SLC25A4 ZYX LGALS9 FAM110C MYO5B PPFIBP2 DYSF TMEM56 FOXO4 HOXA11 IL4R HSPCB PBK WISP2 FOXO4 SERPINB8 COL22A1 KLK13 TMEM38B KRT6A WT1 NUDT11 GAS6 CD68 CDC20 UGT2B15 ABCC13 AURKB CLIC6 CSR2BP CTPS1 DEPDC1B PCP4	PPP1CB DNAJB14 FOXO4 FOXO1 PFKFB2 SH3BGRL TRIM13 WT1 COL22A1 KLK13 CACNG4 CHRNE CACNG4 CNN2 DYSF FAM110C MYO5B PPFIBP2 FAM110C LGALS9 CYP3A4 CYP2B6 DNAJB14 CYP2B6 PLXNA2 SLC45A2 KCNH2 PLLP SLC25A4 ZYX PDZD2 TMEM56 HOXA11 ALDOA CREB3L1 RNASEL MAP7 MYT1 SERPINB8 BRMS1 EPB41L3 P2RY14 PBK IL4R PLXNA2 KLK7 S100A9 PBK SLC4A11 GAL MAP3K8 MT1L ABAT	AURKA MAP7 WT1 CYP3A4 COL22A1 KLK13 CD68 BRMS1 MAP7 TRIM13 NUDT11 HMGCR PFKFB2 SH3BGRL FOXO4 CACNG4 CHRNE CNN2 HOXA11 BRMS1 S100A9 PPP1CB DYSF FADS1 DNAJB14 CYP2B6 KCNH2 PLXNA2 SLC45A2 KCNH2 PLLP SLC25A4 ZYX FADS1 CAMKK2 CREB3L1 RNASEL WT1 SLC45A2 COL22A1 KLK13 EPB41L3 CNN2 DYSF FAM110C PBK MYO5B PPFIBP2 FOXO4 LGALS9 SFRP1 BCAS1 GNMT ABAT ERMP1 MSX2 SERPINB8	SQLE IL4R PLXNA2 SERPINB8 FAM49A CD68 BRMS1 MAP7 TRIM13 NUDT11 PFKFB2 SH3BGRL TRIM13 CACNG4 CHRNE CNN2 HOXA11 BRMS1 NUCB2 DNAJB14 APPBP2 GNMT PLA2G6 ITGA6 PLLP MAP7 AURKA FADS1 CAMKK2 CREB3L1 RNASEL WT1 SLC45A2 COL22A1 KLK13 EPB41L3 CNN2 DYSF FAM110C MYO5B PPFIBP2 FOXO4 LGALS9 SFRP1 BCAS1 TMEM56 CHEK1 HMGCR TMEM3	TCF12 SMPD1 VASP OGG1 CASP2 FTL FGFR1 PCDH17 ERBB2 COL22A1 KLK13 LGALS9 WT1 LST1 S100A9 GAS6 HMGCR FOXO1 PLA2G6 ITGA6 MT1L MAP7 AURKA FADS1 CAMKK2 CREB3L1 RNASEL WT1 SLC45A2 COL22A1 KLK13 EPB41L3 CNN2 DYSF FAM110C MYO5B PPFIBP2 FOXO4 LGALS9 SFRP1 BCAS1 TMEM56 CHEK1 HMGCR TMEM3	TCF12 SMPD1 VASP OGG1 CASP2 FTL FGFR1 PCDH17 ERBB2 COL22A1 KLK13 LGALS9 WT1 LST1 S100A9 GAS6 HMGCR FOXO1 PLA2G6 ITGA6 MT1L MAP7 AURKA FADS1 CAMKK2 CREB3L1 RNASEL WT1 SLC45A2 COL22A1 KLK13 EPB41L3 CNN2 DYSF FAM110C MYO5B PPFIBP2 FOXO4 LGALS9 SFRP1 BCAS1 TMEM56 CHEK1 HMGCR TMEM3	CEP72 TCF12 DSTN NOTCH1 RRM2B TMEM3 KDELC1 8B KDELC1 FAM171 A1 HSPA12 A FAM171 LIM2 MAP3K7 IP3 NKAIN1 PQLC3 RPPH1 SEMA3 G SLC37A 2 STBD1 TMEM2 TRIM21 WNT11 ZIC2 TMEM3 8B HES1 CD151 ELOVL1 GAL3ST 1 GCOM1 KAT2B PLEKH M1 SLC20A 1 CMBL CTTN SLC4A1 1 ANKRA 2 IGDCC4	CEP72 TCF12 DSTN RRM2B TMEM3 KDELC1 8B KDELC1 PGM2 NOTCH1 HES1 FAM171 A1 HSPA12 A LIM2 MAP3K7 IP3 NKAIN1 PQLC3 RPPH1 SEMA3 G SLC37A 2 STBD1 TMEM2 TRIM21 WNT11 ZIC2 SLC20A 1 CMBL CD151 ELOVL1 GAL3ST 1 GCOM1 KAT2B PLEKH M1 SLC20A 1 CMBL CTTN SLC4A1 1 ANKRA 2 IGDCC4	CEP72 TCF12 DSTN KDELC1 PGM2 TMEM3 8B NOTCH1 RRM2B HES1 FAM171 A1 HSPA12 A LIM2 MAP3K7 IP3 NKAIN1 PQLC3 RPPH1 SEMA3 G SLC37A 2 STBD1 TMEM2 TRIM21 WNT11 ZIC2 CD151 ELOVL1 GAL3ST 1 GCOM1 KAT2B PLEKH M1 SLC20A 1 CMBL CTTN GFRA1 ANKRA 2 IGDCC4 THAP10

		APPBP2 MAP3K8 BMPRI1B CYP2S1 GBP1 SFTPBP PSAP MAP7 FADS1 S100A9 BRMS1 ITGA6 TSKU ALDOA CA2 ENC1	PTGER3 SAC3D1 SFXN2 SLC39A8 FOXC1 EPB41L3 SLC45A2 TRIOBP MCM6 MCM7 KLK7 TK1 ERBB2 C8ORF4 CYP2S1 SCGB2A1 BLM BMPRI1B KIAA0101 GMNN PLK4 GFRA1 NUCB2 GAL SLC4A11 FANCI TRIP13 ARL3 CENPA FBXO5 GINS2 KIF11 KIF15 NCAPD2 PLOC1 PRIM1 TACC3 UBE2T TSKU FADS1 ATAD2 CENPF HMGB2 KIF20A KIF4A SMC2 APPBP2 ECT2 IGFBP2 HES2	ERMP1 MSX2 SFRP1 C8ORF4 ENC1 FOXC1 HMGCR CYP2S1 EXOSC4 ITGA6 KRT6A FADS1 AURKA	IL4R SFRP1 FOXO1 EPB41L3 ABCA1 PDZD2 NUCB2 CDC20 SLC4A11 MT1L	CDC42EP3 KLK2 TRIOBP ABAT ERMP1 MSX2 PDZD2 FOXO1 HES2 KLK7 SCGB1D2 CISH GAL SLC4A11 HOXA11 NRTN ALDOA FOXC1 ENC1 ITGA6			THAP10 C1ORF6 3 BLM MOD2 PFKFB2 SH3BGR L TRIM13 GAS6 OGG1 FDXR AHRR SFRP1 RPS6KA 3 GALR2 UBE3B COX5B FAM46B S100A13 RGL1 SLC39A 4 GFRA1 ETFB PLK3 SMPD1 CYP2S1 TRIOBP CDT1 MASTL MCM10 IER5L ERBB2 ABCC13 AURKB CLIC6 CSR2P2B P CTPS1 DEPDC1 B PCP4 PTGER3 SAC3D1 SFXN2 SLC39A 8 GFRA1 ETFB PLK3 SMPD1 CYP2S1 TRIOBP CDT1 MASTL MCM10 IER5L ERBB2 ABCC13 AURKB CLIC6 CSR2P2B P CTPS1 DEPDC1 B PCP4 PTGER3 SAC3D1 SFXN2 SLC39A 8 SH3RF1	IGDCC4 THAP10 GFRA1 C1ORF6 3 OGG1 CDT1 MASTL MCM10 MOD2 ABCC13 AURKB CLIC6 CSR2P2B P CTPS1 DEPDC1 B PCP4 PTGER3 SAC3D1 SFXN2 SLC39A 8 MCM6 MCM7 PPP1R14 C COX5B UBE3B GMNN PLK4 GAS6 AHRR TRIOBP RNFT2 FAM122 A COX5B GALR2 FAM46B S100A13 TRIP13 CDT1 MASTL MCM10 RNFT2 PLK3 SFRP1 RACGA P1 FAM46B S100A13 PFKFB2	SLC4A1 1 BLM C1ORF6 3 SMPD1 EID1 MOD2 FDXR OGG1 AHRR PFKFB2 SH3BGR L TRIM13 RPS6KA 3 GAS6 ABCC13 AURKB CLIC6 CSR2P2B P CTPS1 DEPDC1 B PCP4 PTGER3 SAC3D1 SFXN2 SLC39A 8 UBE3B FAM122 A COX5B GALR2 FAM46B S100A13 TRIP13 CDT1 MASTL MCM10 RNFT2 PLK3 SFRP1 RACGA P1 ARL3 CENPA
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			TMEM97 RACGAP1 GNMT CMBL SFRP1 MITF CAMKK2 PPP2R2C MAP7 MYBL2 SLC6A14 CXCL11 PPARGC1A FOXO1 ALOX15B AMACR RNF103 OLFM1 CHEK1 PDZD2 S100A9 UGT2B7 CYP3A4 SLC2A4 HPGD CKS1B GBP1 CDC42EP3 ITPK1 ID1 TMPRSS2 BCAS1 PPL SAA2 SQLE MT1L KLK2 H6PD HSD11B1 ALPK3 HHIPL2 STAT5A PSMD6 DENND5A MPHOSPH9 PLXNA2 CDT1 MASTL MCM10 TBC1D1						TSKU HIVEP1 PBK TRIP13 ARL3 CENPA FBXO5 GINS2 KIF11 KIF15 NCAPD2 PLOD1 PRIM1 TACC3 UBE2T RACGA P1 RNFT2 ECT2 VNN1 CASP2 ITGA6	SH3BGR L TRIM13 ARL3 CENPA FBXO5 GINS2 KIF11 KIF15 NCAPD2 PLOD1 PRIM1 TACC3 UBE2T RGL1 SLC39A 4 ETFB ECT2 TSKU PBK CBFA2T 3 KCNJ5 EID1 PLK3 CBR1 IGFBP2 CHEK1 NRTN IER5L MLPH HIVEP1 PON1 SFRP1 MSMB ADAMT S9 SH3RF1 PGR ITGA6 CKS1B CDC20 SMPD1 CA2 CYTH1 VNN1 AURKA	FBXO5 GINS2 KIF11 KIF15 NCAPD2 PLOD1 PRIM1 TACC3 UBE2T TSKU CYP2S1 ERBB2 PBK ETFB RGL1 SLC39A 4 ECT2 TRIOBP CBR1 MCM6 MCM7 CYTH1 WISP2 PPP1R14 C IER5L GMNN PLK4 SH3RF1 HIVEP1 PGR NRTN CKS1B CDC20 VNN1
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			CA2 ST3GAL1 GPRC5A OLFML3 DLX4 RPS6KA3 TACC1 ABAT ERMP1 MSX2 CENPN PDSSB SOCS2 SHBG PTGER4 SFTPB SCGB1D2 SCNN1A HMMR BRMS1 CITED2 FAM49A UBE2C TFF3 ITGAM GGH STMN1								
Downregulated mRNA	NSF SESN1 HIG2 SLTM ZBTB43 MYNN ADORA2B CDCA4 CENPJ DNAJC9 DONSON HAUS8 MCMBP NUP155 PARP2 RMI1 SCARA3 SLC16A14 SUV39H2 TMEM194A PPIH CTSL2 GPR19 LFNG MIR20B NUP54	TMSB15A MYNN C9ORF40 ADORA2B CDCA4 CENPJ DNAJC9 DONSON HAUS8 MCMBP NUP155 PARP2 RMI1 SCARA3 SLC16A14 SUV39H2 TMEM194A PPIH CTSL2 GPR19 LFNG MIR20B NUP54	ADORA2B CDCA4 CENPJ DNAJC9 DONSON HAUS8 MCMBP NUP155 PARP2 RMI1 SCARA3 SLC16A14 SUV39H2 TMSB15A MYNN C9ORF40 TMEM194A MAST4 MSH5 TREX1 CTSL2 GPR19 LFNG	MYNN TMSB15A NOP56 ADORA2B CDCA4 CENPJ DNAJC9 DONSON HAUS8 MCMBP NUP155 PARP2 RMI1 SCARA3 SLC16A14 SUV39H2 C9ORF40 PPIH HIG2 TMEM194A LBR SLTM ZBTB43	SESN1 MYNN HIG2 SLTM ZBTB43 AKR1C3 TRAF5 ADORA2B CDCA4 CENPJ DNAJC9 DONSON HAUS8 MCMBP NUP155 PARP2 RMI1 SCARA3 SLC16A14 SUV39H2 TMSB15A CAPRIN1	SESN1 GEMIN4 RPS19 NAP1L1 TNPO2 NME2 ASPH NSF ADORA2B CDCA4 CENPJ DNAJC9 DONSON HAUS8 MCMBP NUP155 PARP2 RMI1 SCARA3 SLC16A14 SUV39H2 MYNN TMSB15A	ADAM19 CCL5 NOP56 CAPRIN1 TRAF5 SDC4 TBL1XR1 LGALS1 C9ORF40 UBE2M FKBP5 NPM1 CXCL10 SAP18 TNFRSF10B B CCDC93 STX1A HK2 DEK H1FX HIG2 ZFAND5	ADAM19 CCL5 NOP56 CAPRIN1 TRAF5 SDC4 TBL1XR1 LGALS1 C9ORF40 UBE2M FKBP5 NPM1 CXCL10 SAP18 TNFRSF10B STX1A HK2 DEK H1FX HIG2 ZFAND5 NAP1L1	DMXL1 OLFML1 TUBGCP 3 TBC1D9 C9ORF4 1 APT RSBN1 TEFM HIG2 MAPK8 ADAM1 9 SDC4 OSBP2 GSS DEK STEAP1 MAN1A 2 YPEL5 LRP6	DMXL1 OLFML1 TUBGCP 3 TBC1D9 C9ORF4 1 APT RSBN1 TEFM HIG2 GSS MAPK8 LRP6 YPEL5 SDC4 STEAP1 OSBP2 DEK ADAM1 9 MAN1A 2	DMXL1 OLFML1 TUBGCP 3 APT RSBN1 TBC1D9 C9ORF4 1 TEFM LRP6 ADAM1 9 MAPK8 HIG2 OSBP2 SDC4 ABCA13 ABCC13 TMEM5 9L YPEL5 STEAP1

	MAST4 MSH5 TREX1 NOP56 PPIH TNPO2 RPS19 C9ORF40	PRR16 SP4 MAST4 MSH5 TREX1 CBX2 GART LBR SESN1 RPS19 ASPH TNPO2 GEMIN4 NAP1L1 DEK SLTM ZBTB43 HIG2 NOP56 POC1A EFNB2 NME2 TANC1 NDE1 BARD1 TSPAN5 NPM1 TAOK3 INCENP GSS CXCR7 TRIM16 HSPA6 TRAF5 GPLD1 DNMT1 CAPRIN1	MIR20B NUP54 PRR16 SP4 GART NOP56 CBX2 RPS19 SEC16A PPIH TBC1D9 GEMIN4 HPSS SESN1 AKR1C3 YPEL5 ASPH MAPK8 HSPA6 PTPRO EFNB2 PLEC ZBTB10 HIG2 GPLD1 SLC14A1 ABCC5 SLTM ZBTB43 GSS KIAA0256 MXD4 MYH6 TCF25 UGT1A3 BARD1 CD58 LBR WNT7A HEATR3 L1CAM CDK2AP2 NDE1 DEK NPM1 POC1A ELAC2 TANC1 TRIM16 TPM1	CTSL2 GPR19 LFNG MIR20B NUP54 PRR16 SP4 SESN1 MAST4 MSH5 TREX1 CTSL2 GPR19 LFNG MIR20B NUP54 PRR16 GART GSS ASPH TRAF5 EFNB2 RPS19 TNPO2 HSPA6 DEK GEMIN4 POC1A GPLD1 DIO2 SEC16A TANC1 CAPRIN1 NAP1L1 NDE1 AKR1C3 NPM1 DHFR ABCC5 TPM1 BARD1 ERCC2 TBC1D9	TAOK3 WDR77 NAP1L1 NSF TNPO2 MAST4 MSH5 TREX1 CTSL2 GPR19 LFNG MIR20B NUP54 PRR16 SP4 PPIH GART TMEM194 A C9ORF40 RPS19 EFNB2 GEMIN4 CBX2 ASPH ETS1 GART NME2 ZBTB10 PPIH TSPAN5 LBR NDE1 TOB1 POC1A TANC1 BARD1 NOP56	MBNL2 LBR C9ORF40 MAST4 MSH5 TREX1 CXCR7 CTSL2 GPR19 LFNG MIR20B NUP54 PRR16 SP4 PPIH GART CBX2 TMEM194 A SLTM ZBTB43 HIG2 ETS1 NDE1 POC1A ZBTB10 TANC1 TSPAN5 OSR2 INCENP EFNB2 BARD1 TPM1 NPM1	NAP1L1 GPLD1 GART KLF10 KLF10 TOB1 SOD1 TMEM194 A TMSB15A SEC16A WWP2 MAPK8 CXCL2	GPLD1 GART KLF10 TOB1 SOD1 TMEM194A TMSB15A SEC16A WWP2 MAPK8 CXCL2	ITGAV ARNT CADPS2 CCDC41 FNIP2 GCA GPT2 ITPKA KCNJ10 KLHL14 PSD3 GPT2 SPIN3 STARD1 3 ZNF711 PGM2L1 LBR INTU PAQR3 QPCT RNFT1 MBNL2 HK2 ABL1 HEATR3 AIM1 C17ORF 75 COG6 MITD1 PLSCR1 PRKAB2 VPS36 H1FX ABCA13 ABCC13 TMEM5 9L PCOLCE 2 SLC30A 1 ZBTB10 FTSJD1 GUF1 MAP4K4 TNFRSF 10B RASA1 NCOA1	ABCA13 ABCC13 TMEM5 9L ITGAV ARNT CADPS2 CCDC41 FNIP2 GCA GPT2 ITPKA KCNJ10 KLHL14 PSD3 SPIN3 STARD1 3 ZNF711 PGM2L1 MBNL2 HEATR3 AIM1 C17ORF 75 COG6 MITD1 PLSCR1 PRKAB2 VPS36 INTU PAQR3 QPCT RNFT1 LBR NCOA1 PCOLCE 2 FTSJD1 GUF1 HK2 EFNA3 ZBTB10 SLC30A 1 RASA1 MAP4K4	GSS MAN1A 2 DEK MFAP4 EFNA3 ITGAV HK2 TNFRSF 10B SYMPK ABL1 MBNL2 ARNT CADPS2 CCDC41 FNIP2 GCA GPT2 ITPKA KCNJ10 KLHL14 PSD3 SPIN3 STARD1 3 ZNF711 LBR PGM2L1 HEATR3 AIM1 C17ORF 75 COG6 MITD1 PLSCR1 PRKAB2 VPS36 INTU PAQR3 QPCT RNFT1 PCOLCE 2 FTSJD1 GUF1 H1FX PDZK1 FTSJD1 GUF1 MAP4K4
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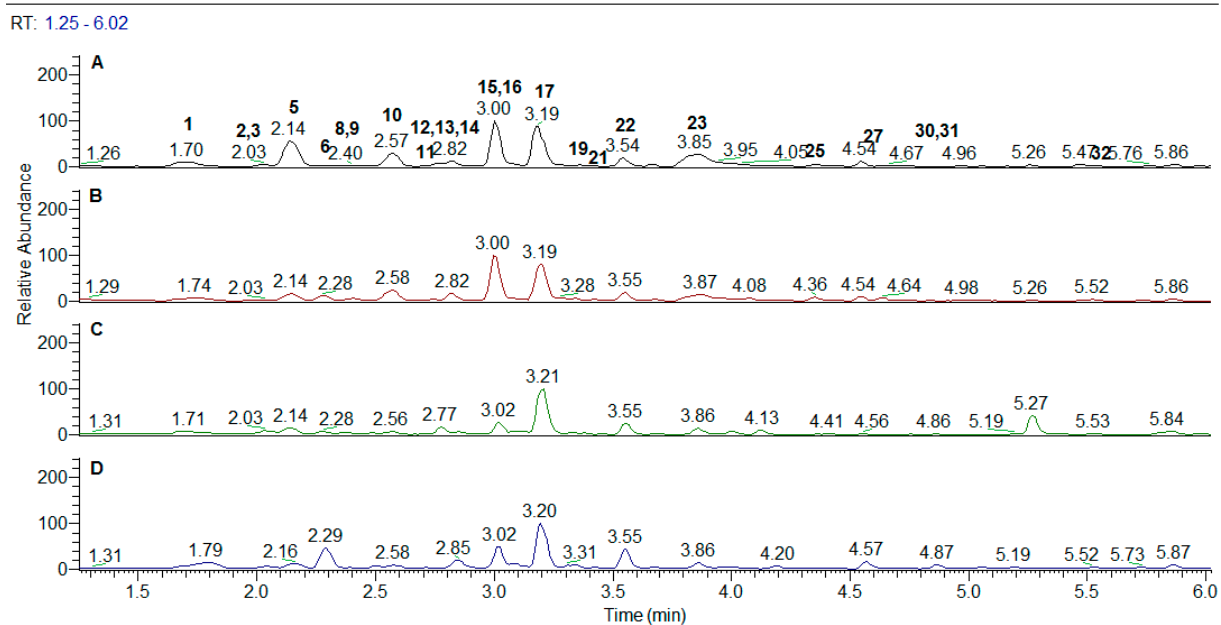
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									SLC16A14 SUV39H2 SIAH1 CUL4B MFAP4 TAOK3 DNMT1 MTIF2 PACSIN2 HSPA5 AHRR CLASP2 CREB3L2 IGF2BP3 PDGFC RAB28 RALA SNX24 TMEM139 MCL1 C9ORF40 SYMPK CD74 IL1R1 BGLAP CHST15 DRG2 FOXN3 IL15 WWC2 HPS5 KIAA0256 MXD4 MYH6 TCF25 UGT1A3 DIAPH2 RAR PDZK1 TRAF5 TMEM121 EFNB2	CYP1B1 WWC2 DNMT1 TMEM121 CUL4B MTIF2 DSPP TAOK3 PACSIN2 HPS5 WNT7A CDK2AP2 FOXN3 AHRR CLASP2 CREB3L2 IGF2BP3 PDGFC RAB28 RALA SNX24 TMEM139 HSPA5 MSI2 ADORA2B CDCA4 CENPJ DNAJC9 DONSON HAUS8 MCMBP NUP155 PARP2 RMI1 SCARA3 SLC16A14 SUV39H2 SIAH1 KIAA0256 MXD4 MYH6 TCF25 UGT1A3 CUL4B HSPA5 AHRR CLASP2 CREB3L2 IGF2BP3 PDGFC RAB28 RALA SNX24 TMEM139 MSI2 TMEM121 CDK2AP2 SLC16A14 SUV39H2 DRG2 OCLN IL1R1 CD74	ADORA2B CDCA4 CENPJ DNAJC9 DONSON HAUS8 MCMBP NUP155 PARP2 RMI1 SCARA3 SLC16A14 SUV39H2 SIAH1 KIAA0256 MXD4 MYH6 TCF25 UGT1A3 CUL4B HSPA5 AHRR CLASP2 CREB3L2 IGF2BP3 PDGFC RAB28 RALA SNX24 TMEM139 MSI2 TMEM121 CDK2AP2 TAOK3 WWC2 TRAF5 IL1R1 DRG2 BGLAP
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									PDGFRL TANC1 CDK2AP 2 RPS19 CAPRIN 1 TOB1	UBE2M BGLAP CHST15 SRCRB4 D HP RARB EFNB2 TRAF5 PDGFRL ASAH1 ZFAND5 RPS19 WDR4 DIO2 CAPRIN 1 PLEC TANC1 TOB1	WNT7A FOXP3 CAPRIN 1 CHST15 RARB EFNB2 SRCRB4 D TOB1 PDGFRL TANC1 WDR4 RPS19 PLEC
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Figure S1. Extracted ion chromatogram of hydroxybenzoic and hydroxycinnamic acids and derivatives in negative ion mode of methanolic extracts from *Achillea wilhemsii* aerial parts (A), *A. allepica* aerial parts (B), *A. wilhemsii* roots (C), *A. allepica* roots (D) (for the compound numbers see Table 2).

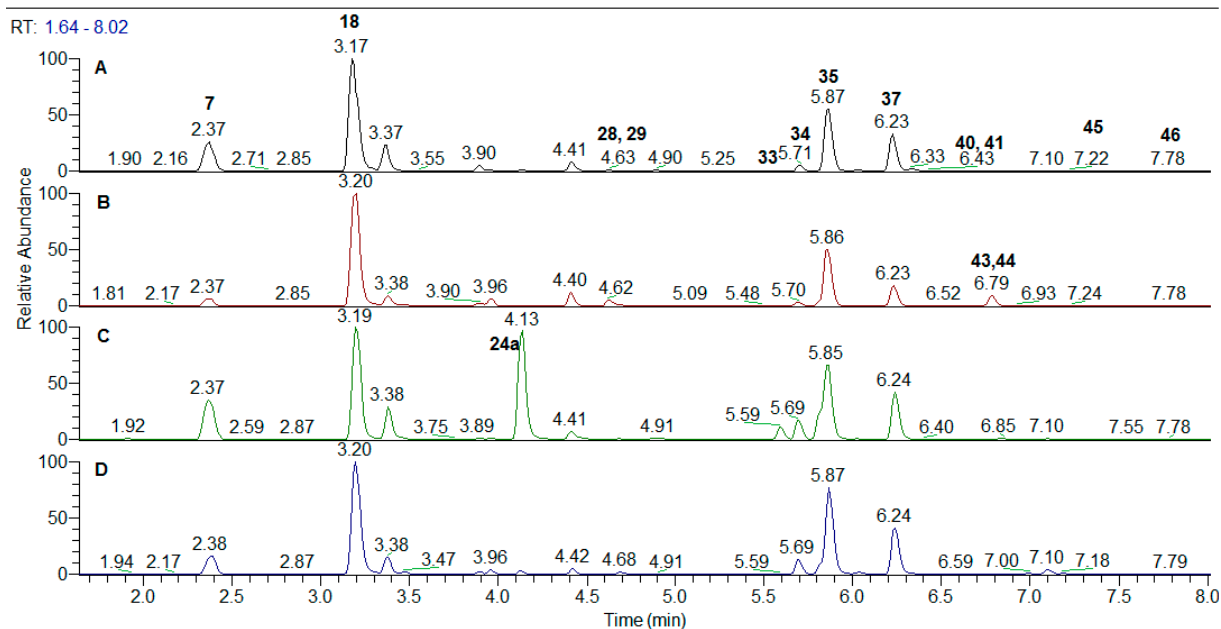


Figure S2. Extracted ion chromatogram of acylquinic acids in negative ion mode of methanolic extracts from *Achillea wilhemsii* aerial parts (A), *A. allepica* aerial parts (B), *A. wilhemsii* roots (C), *A. allepica* roots (D) (for the compound numbers see Table 2).

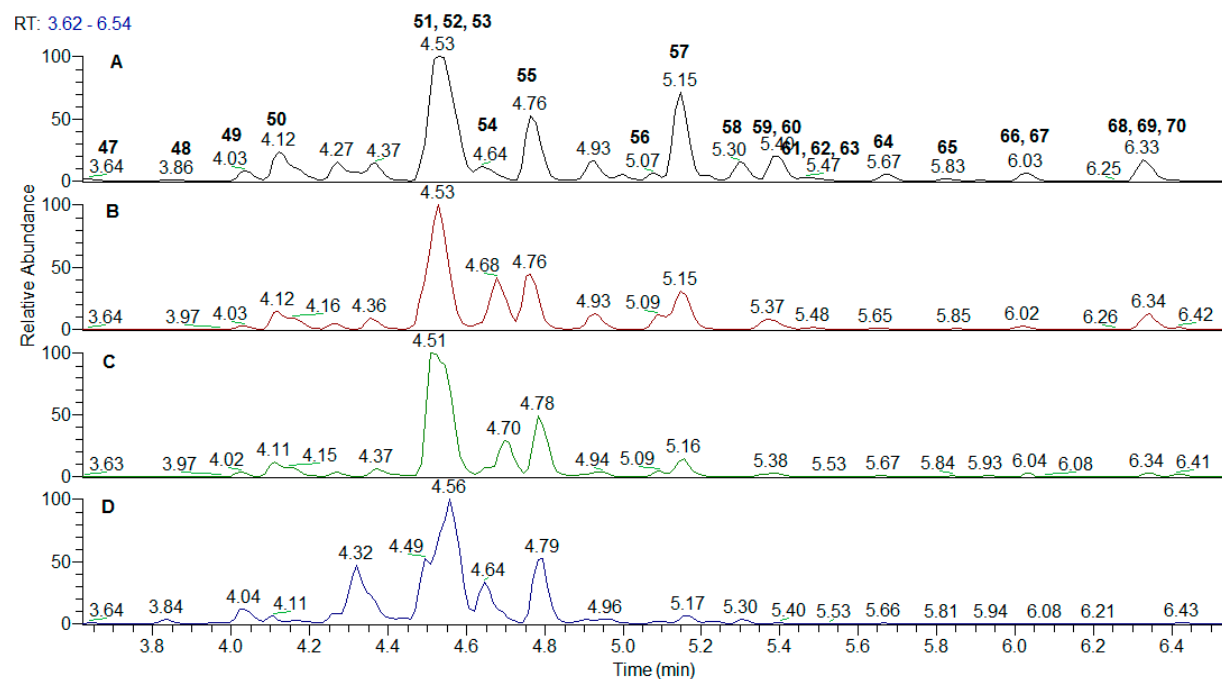


Figure S3. Extracted ion chromatogram of flavonoid glycosides in negative ion mode of methanolic extracts from *Achillea wilhemsii* aerial parts (A), *A. allepica* aerial parts (B), *A. wilhemsii* roots (C), *A. allepica* roots (D) (for the compound numbers see Table 2).

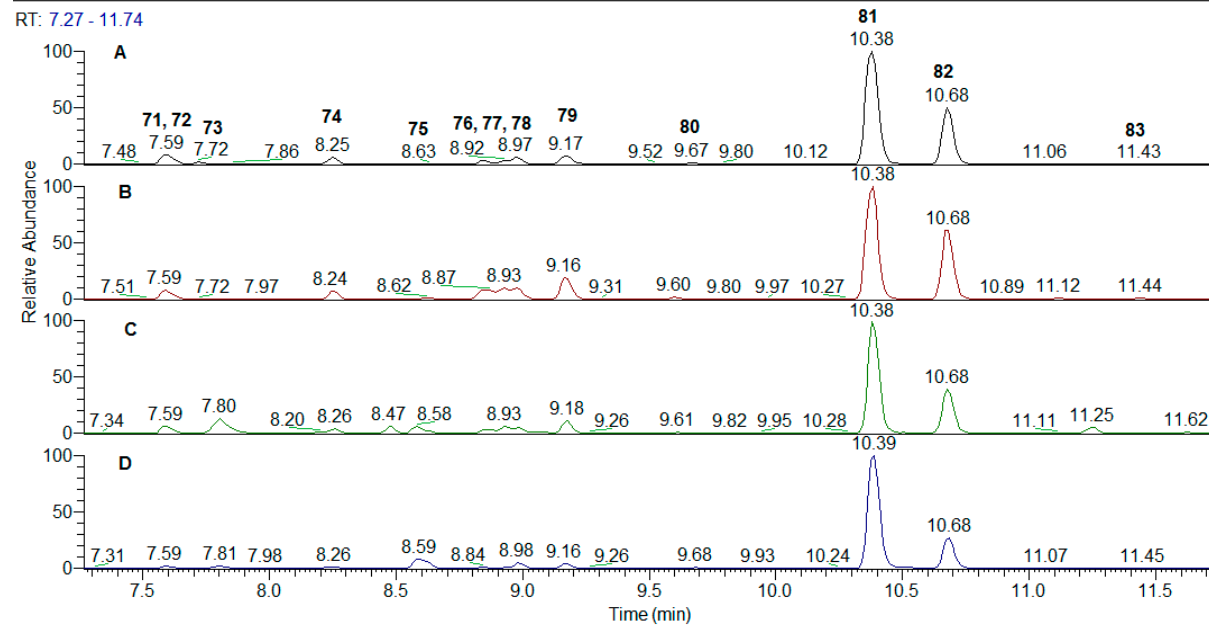
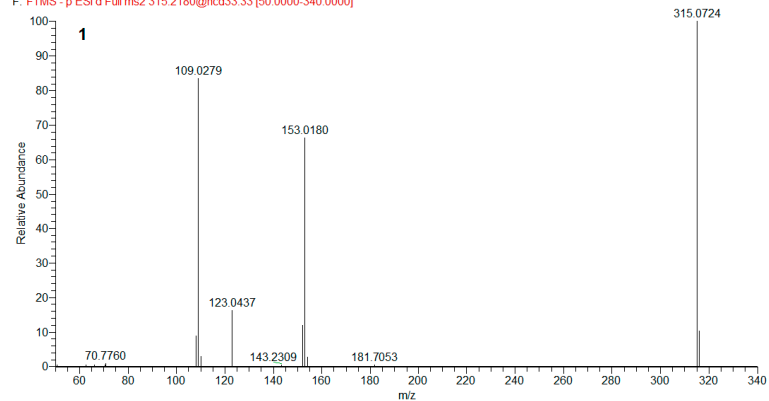
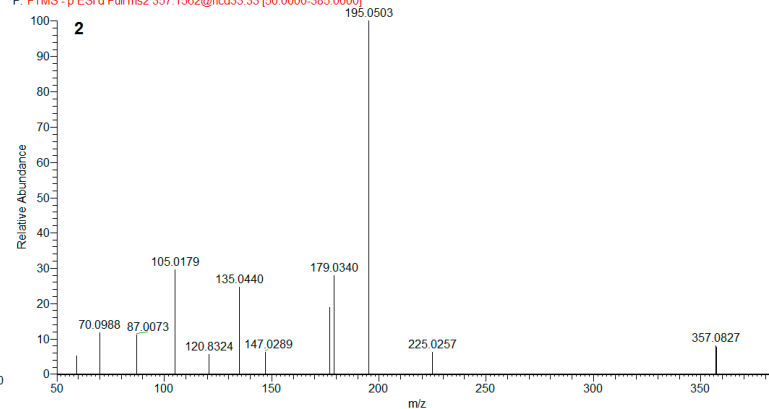


Figure S4. Extracted ion chromatogram of flavonoid aglycones in negative ion mode of methanolic extracts from *Achillea wilhemsii* aerial parts (A), *A. allepica* aerial parts (B), *A. wilhemsii* roots (C), *A. allepica* roots (D) (for the compound numbers see Table 2).

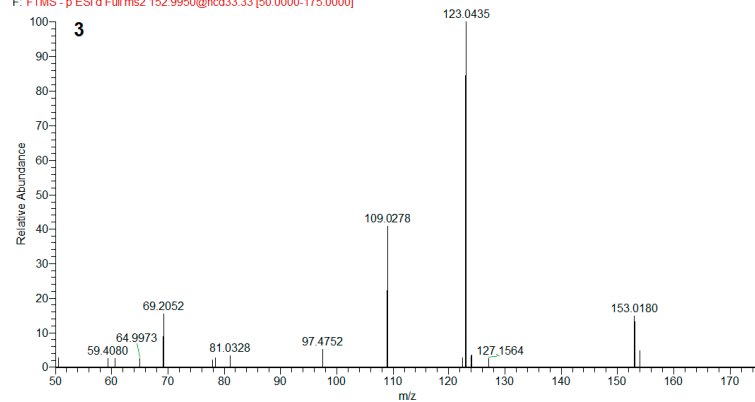
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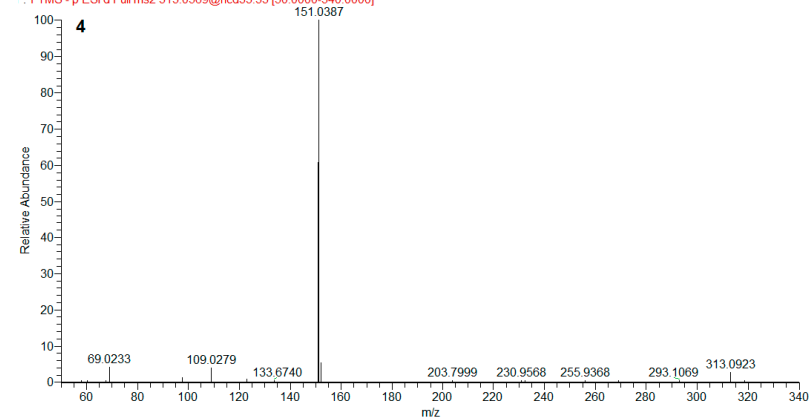
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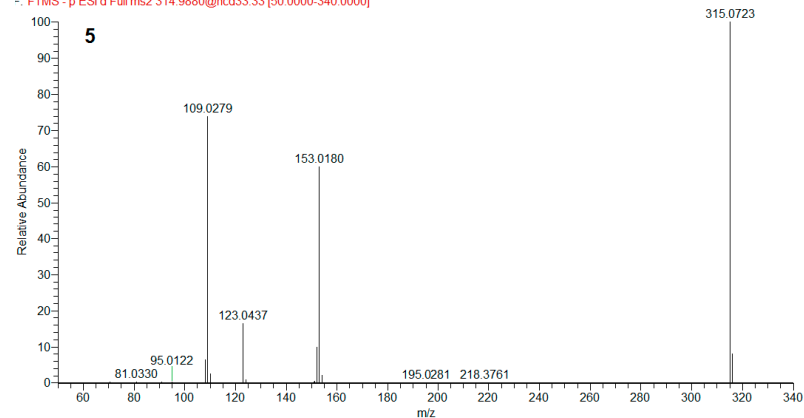
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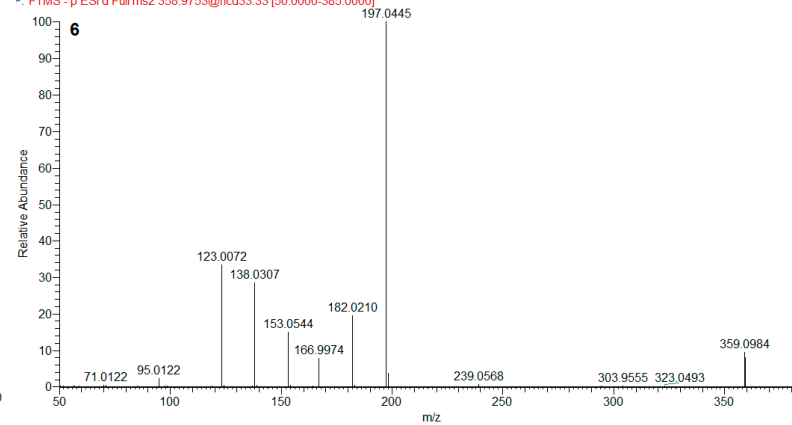
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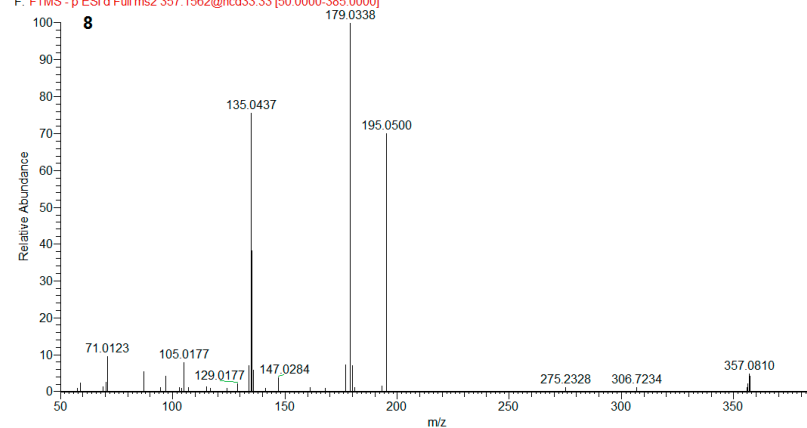
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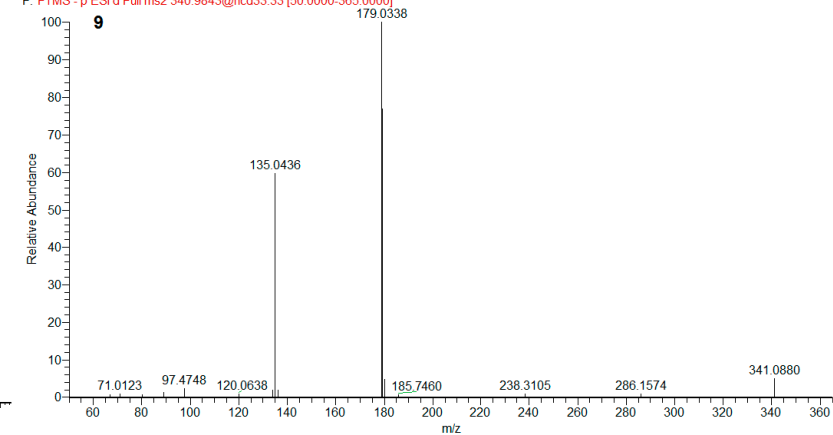
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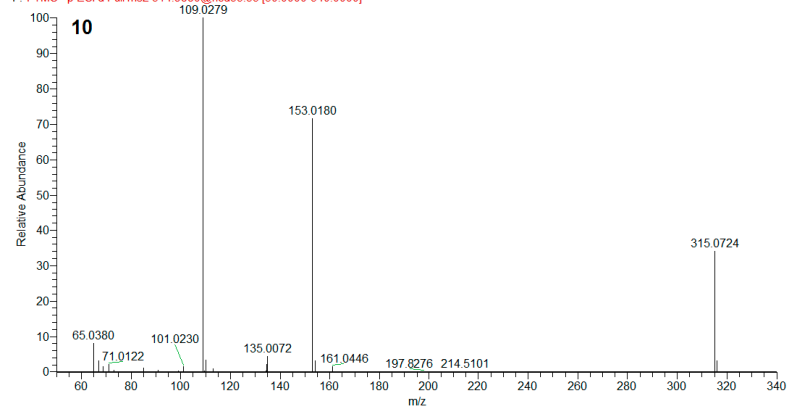
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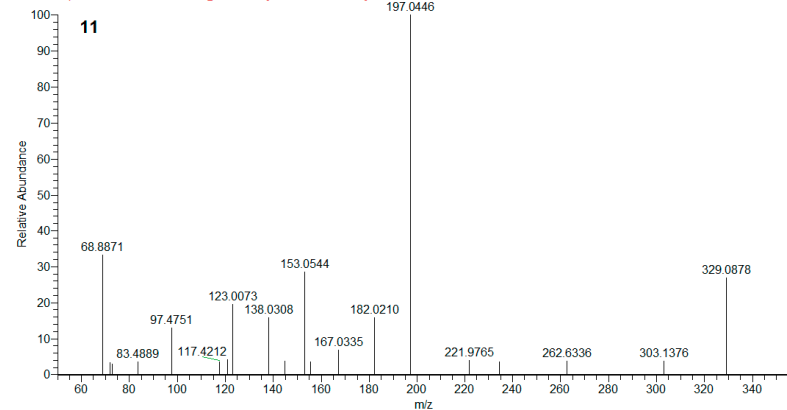
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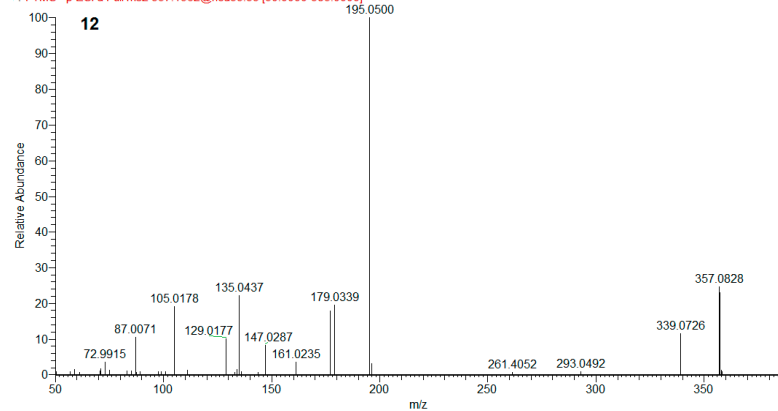
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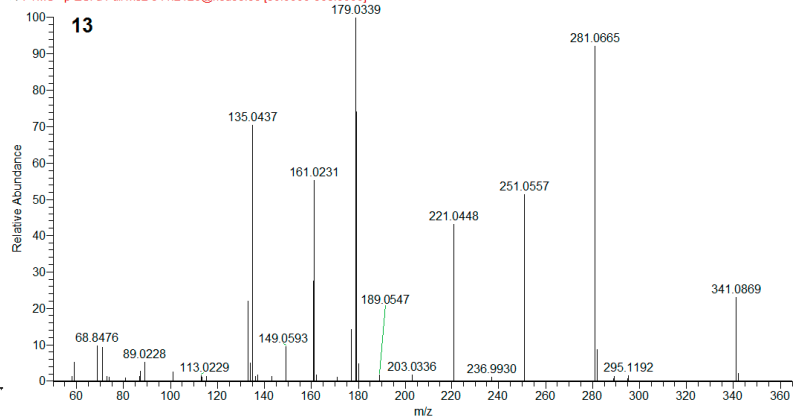
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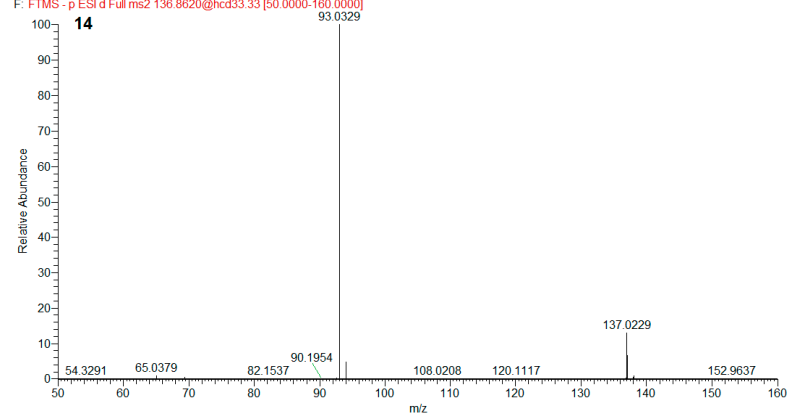
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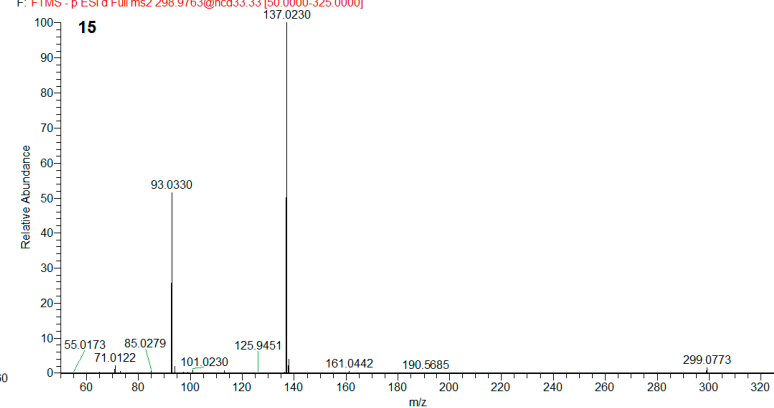
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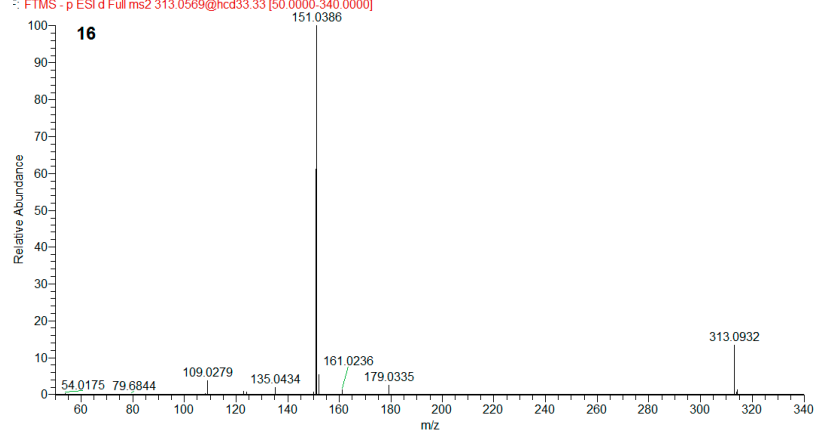
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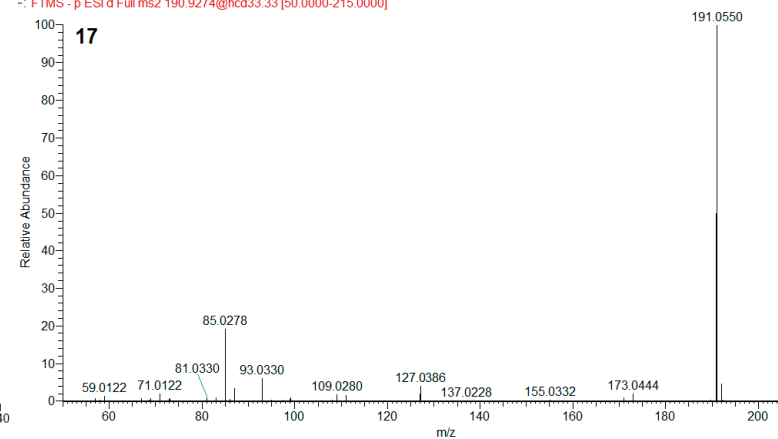
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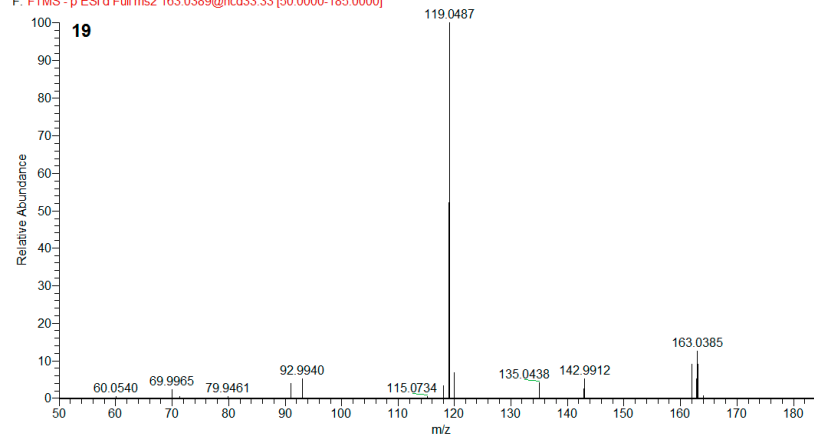
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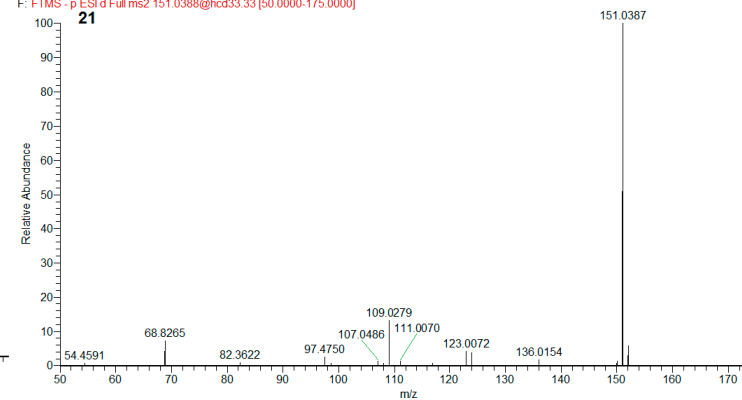
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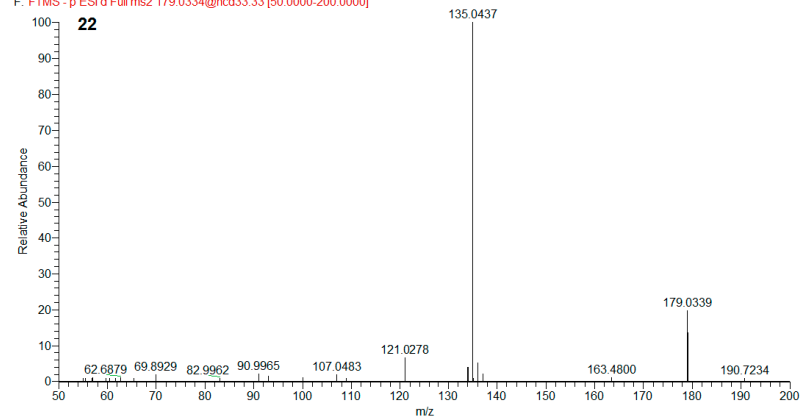
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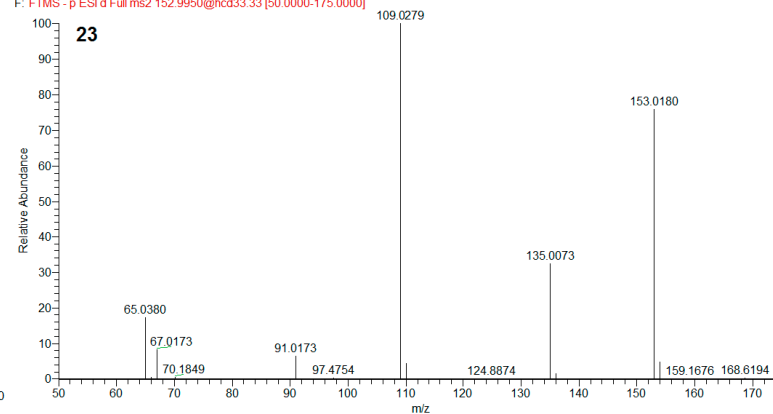
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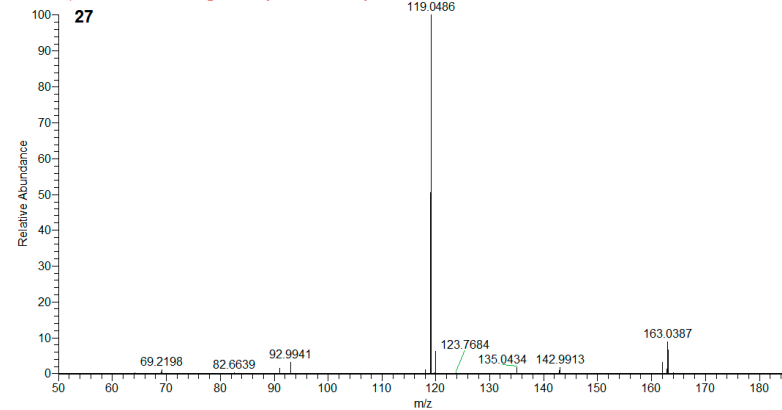
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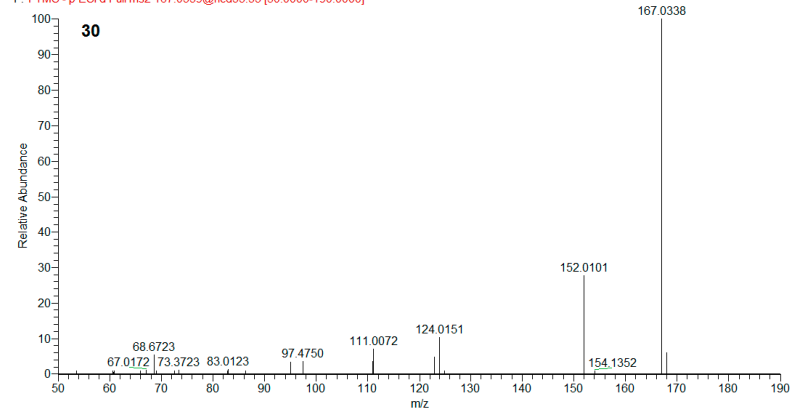
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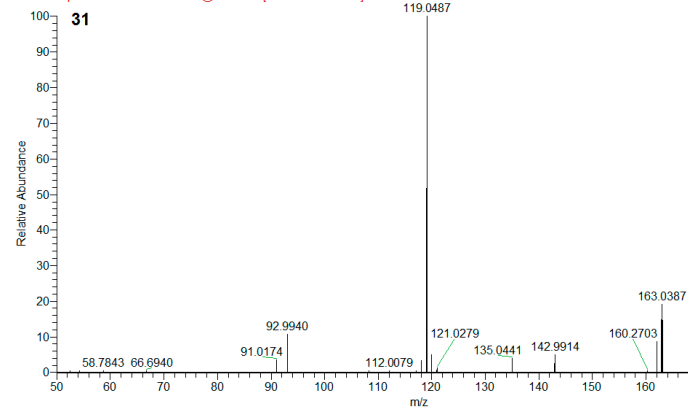
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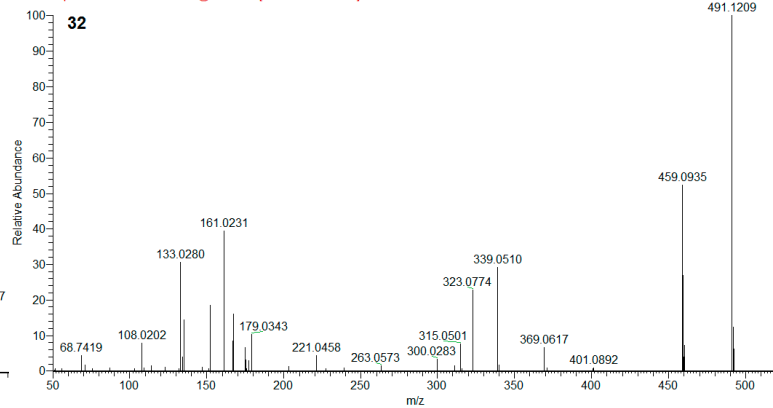
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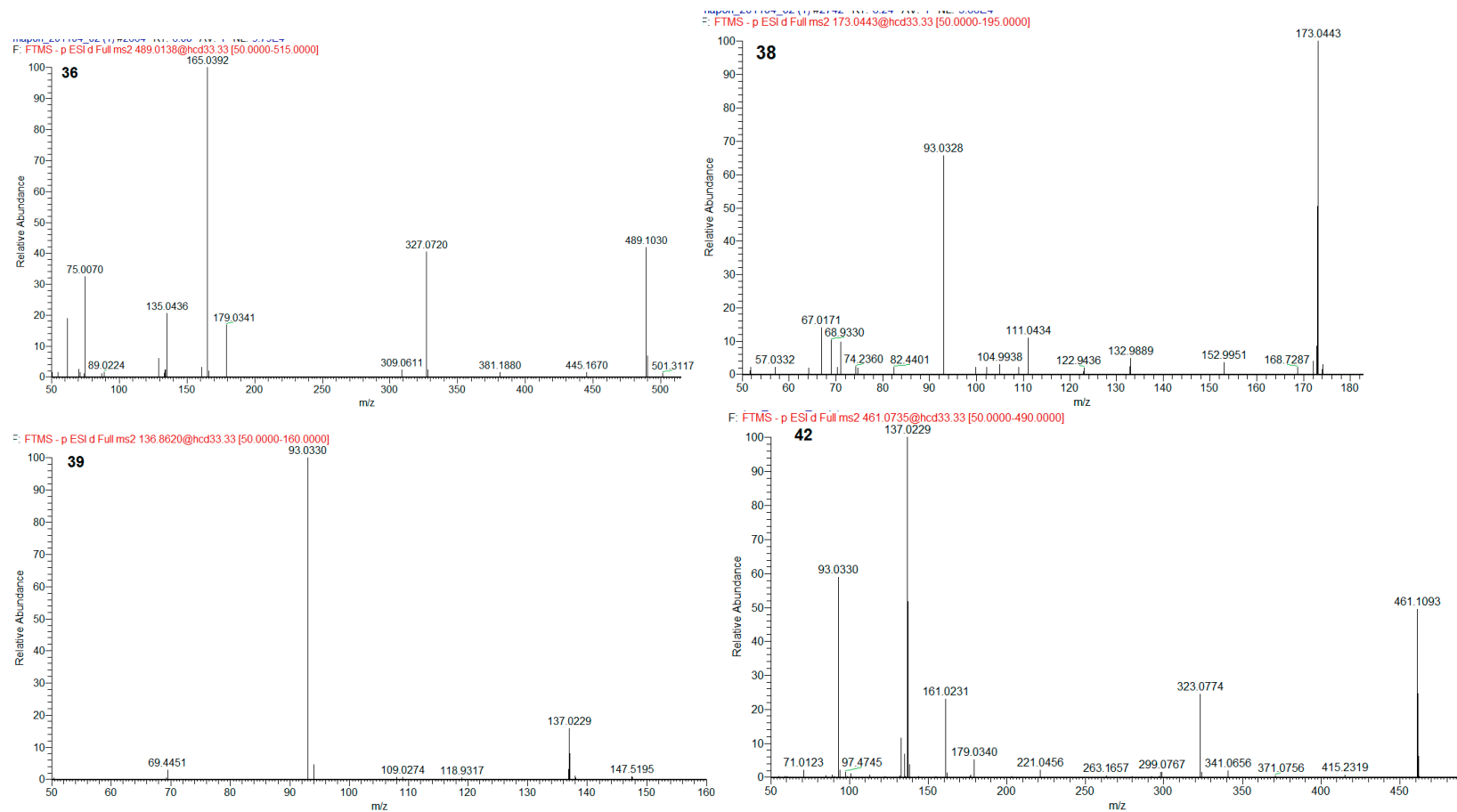
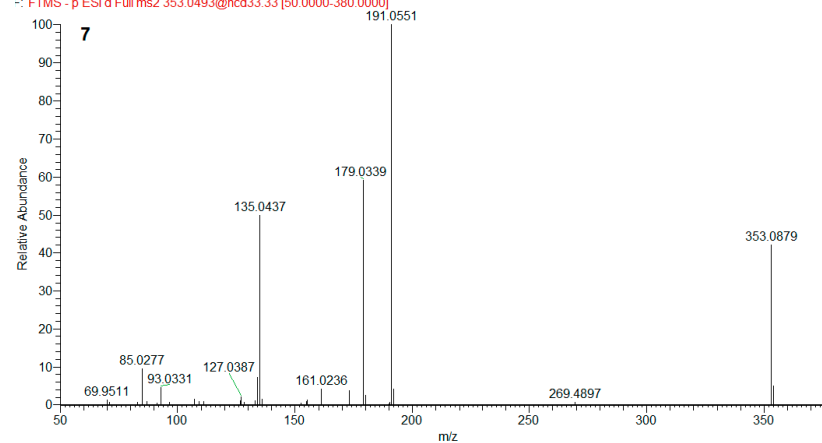
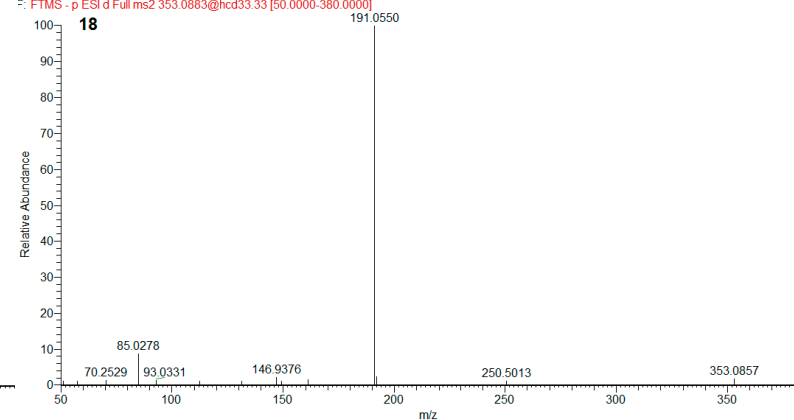


Figure S5. MS/MS spectra of hydroxybenzoic, hydroxycinnamic acids and their glycosides, and sugar esters (for the compound numbers see Table 2).

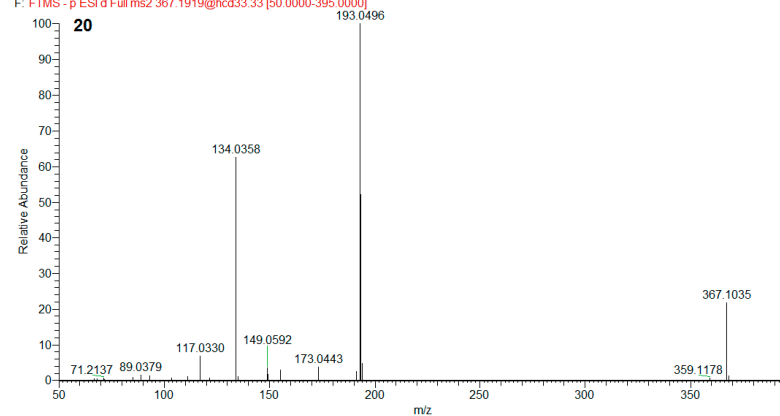
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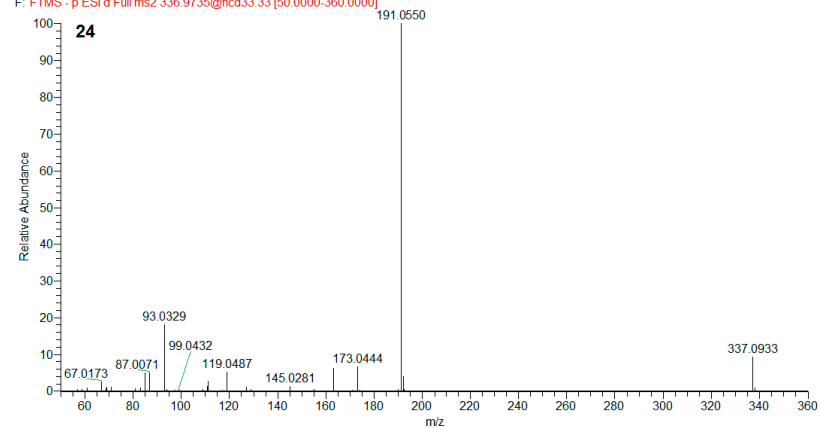
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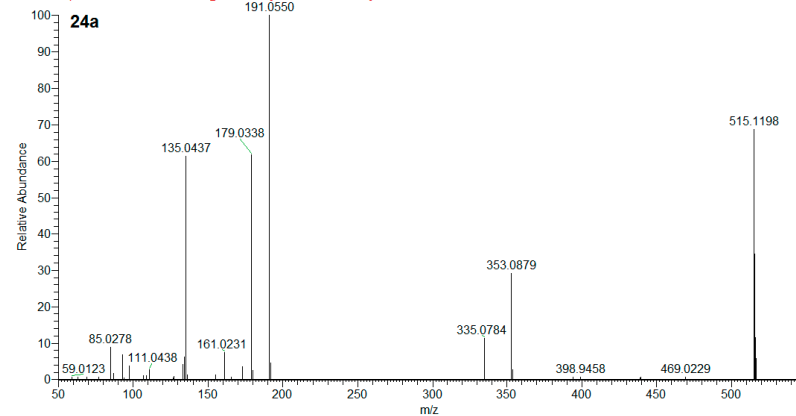
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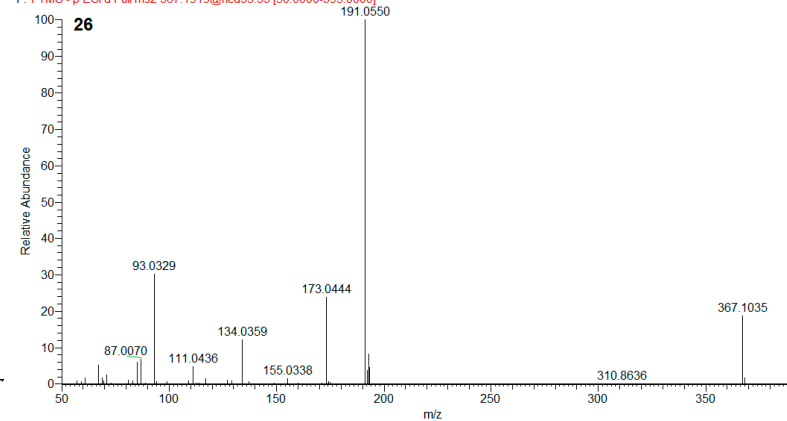
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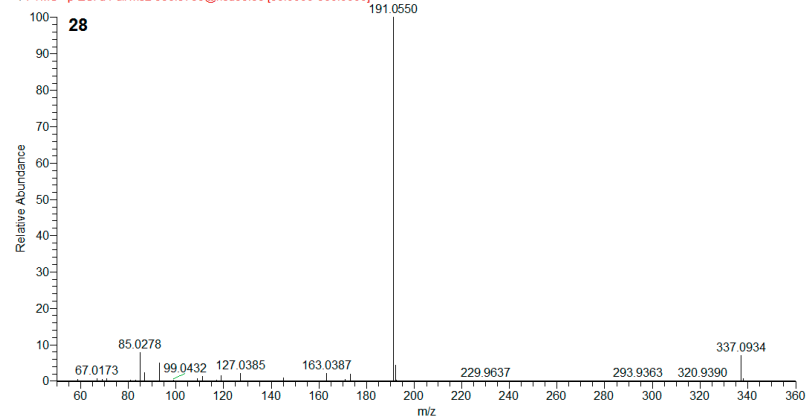
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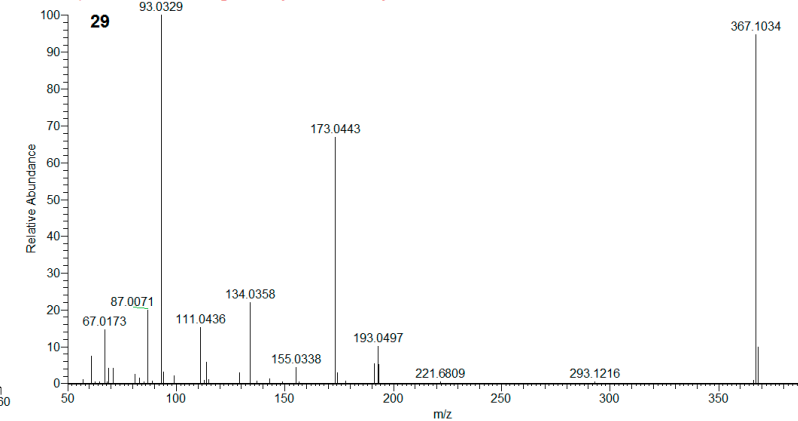
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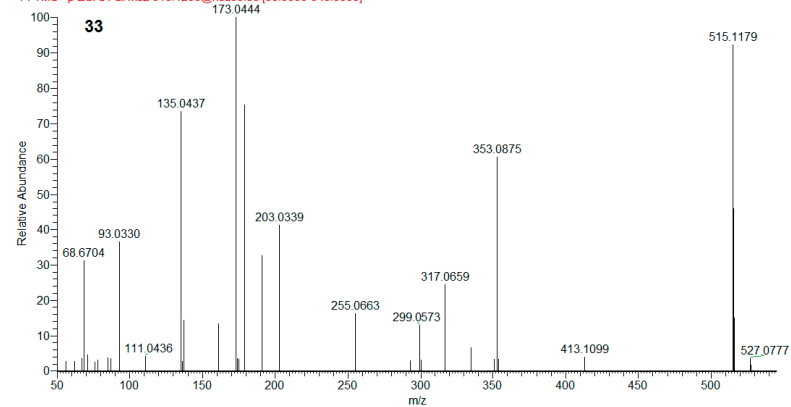
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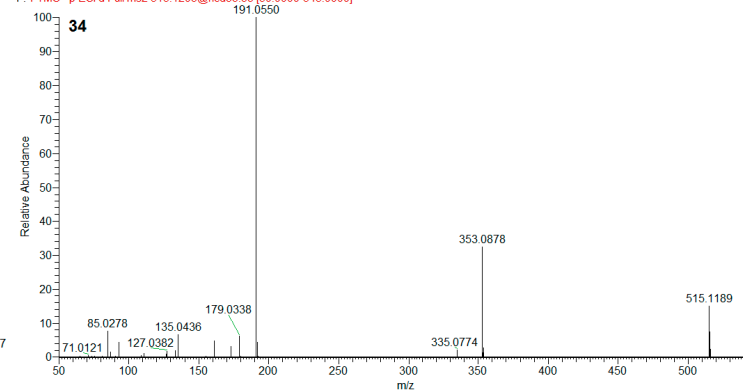
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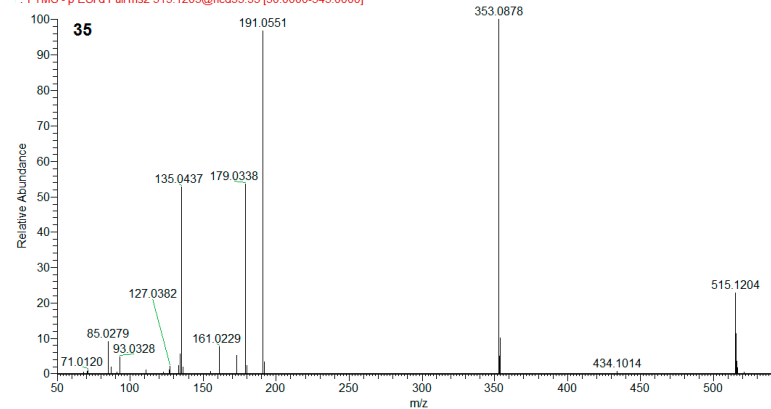
11: FTMS - p ESI d Full ms2 515.1203@hcd33.33 [50.0000-545.0000]



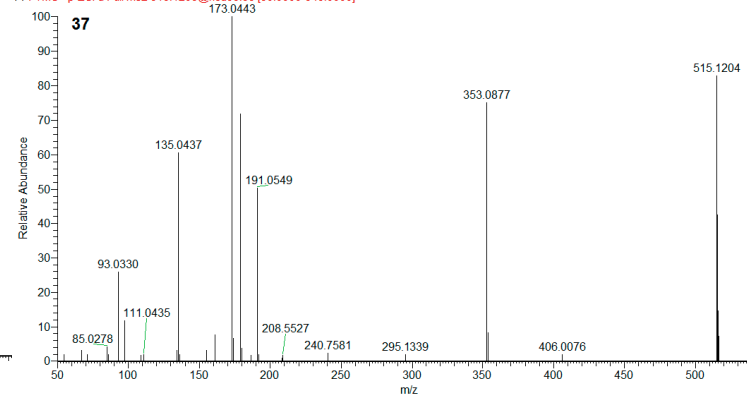
F: FTMS - p ESI d Full ms2 515.1203@hcd33.33 [50.0000-545.0000]



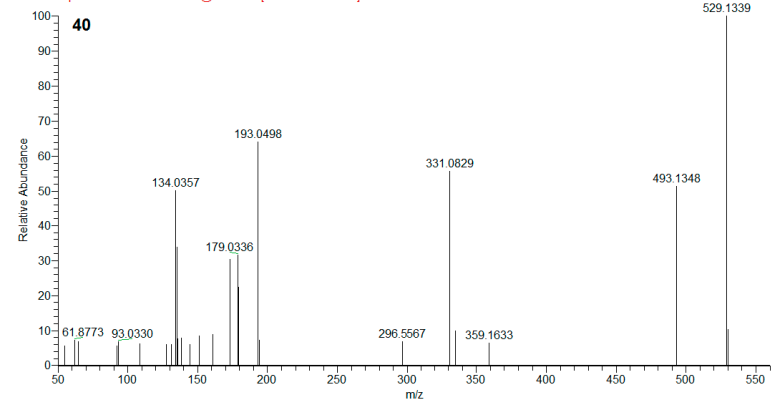
12: FTMS - p ESI d Full ms2 515.1203@hcd33.33 [50.0000-545.0000]



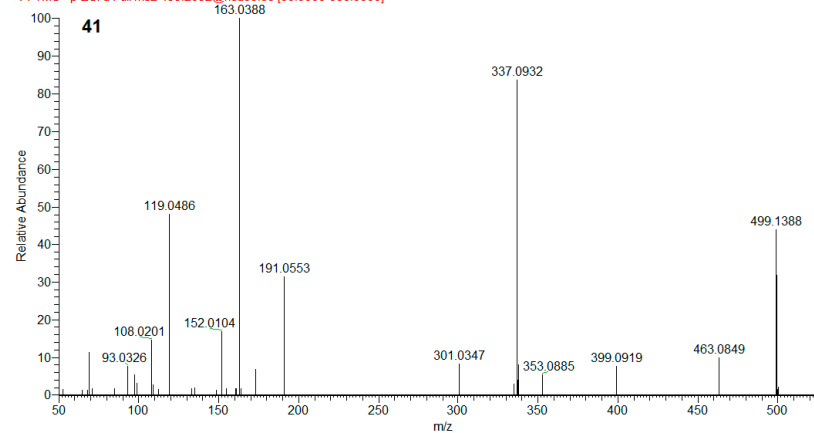
F: FTMS - p ESI d Full ms2 515.1203@hcd33.33 [50.0000-545.0000]



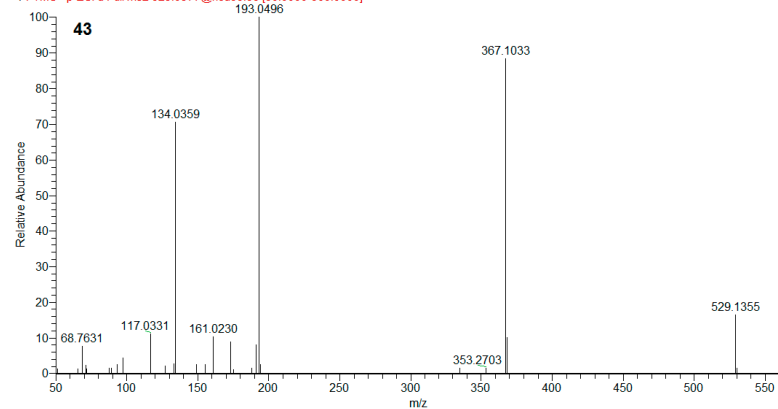
F: FTMS - p ESI'd Full ms2 529.0977@hcd33.33 [50.0000-560.0000]



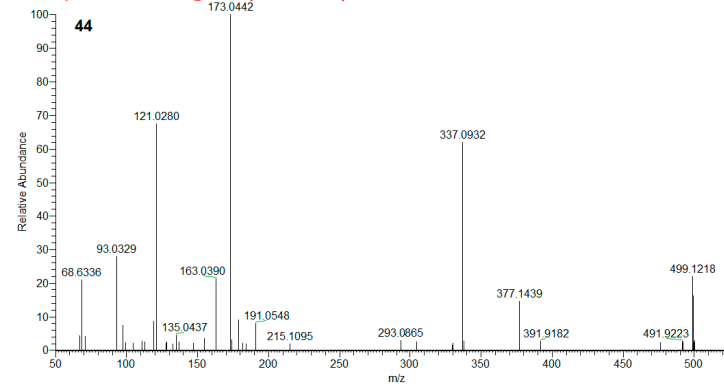
F: FTMS - p ESI'd Full ms2 499.2092@hcd33.33 [50.0000-530.0000]



F: FTMS - p ESI'd Full ms2 529.0977@hcd33.33 [50.0000-560.0000]



F: FTMS - p ESI'd Full ms2 499.2092@hcd33.33 [50.0000-530.0000]



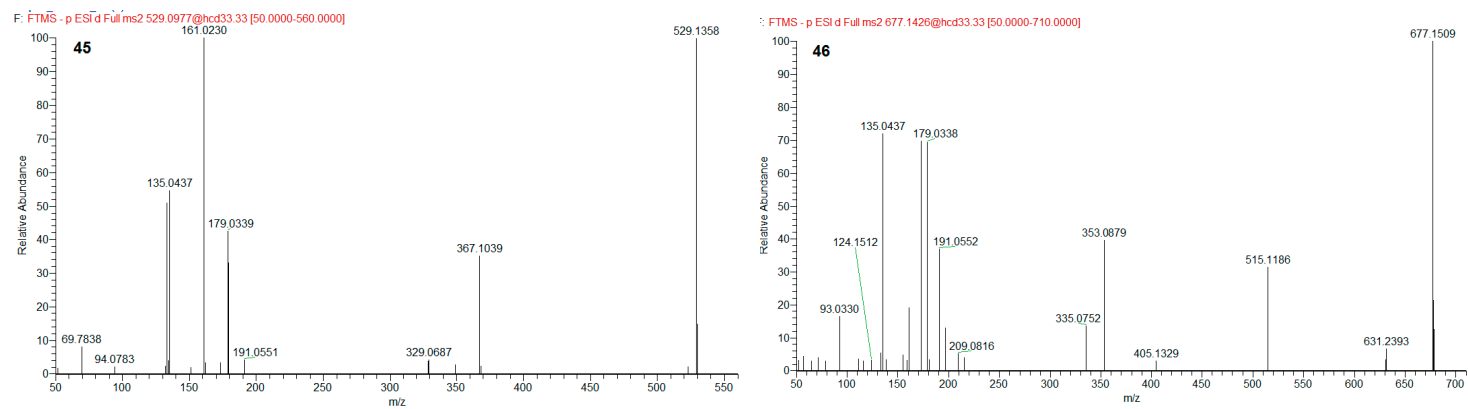
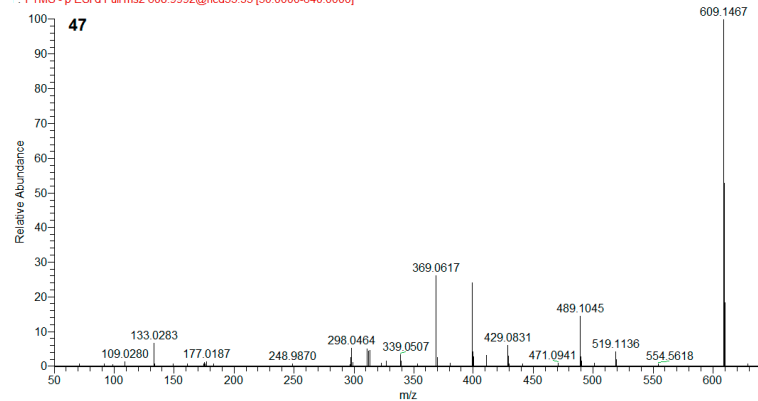
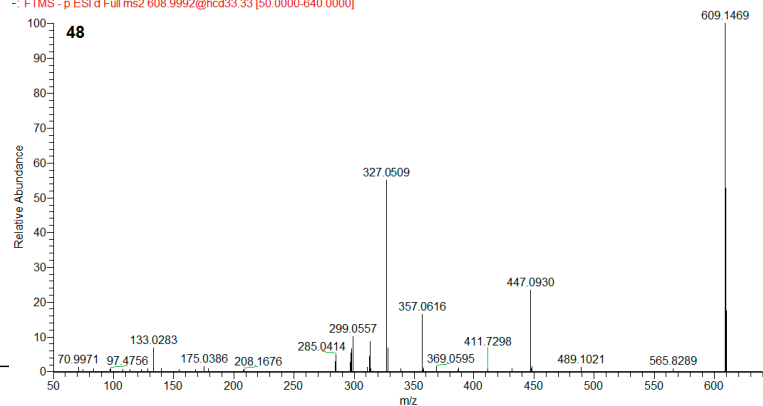


Figure S6. MS/MS spectra of acylquinic acids (for the compound numbers see Table 2).

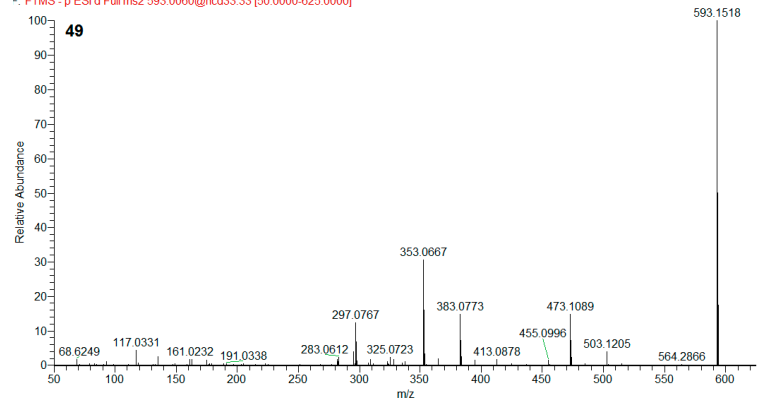
FTMS - p ESI d Full ms2 608.9992@hcd33.33 [50.0000-640.0000]



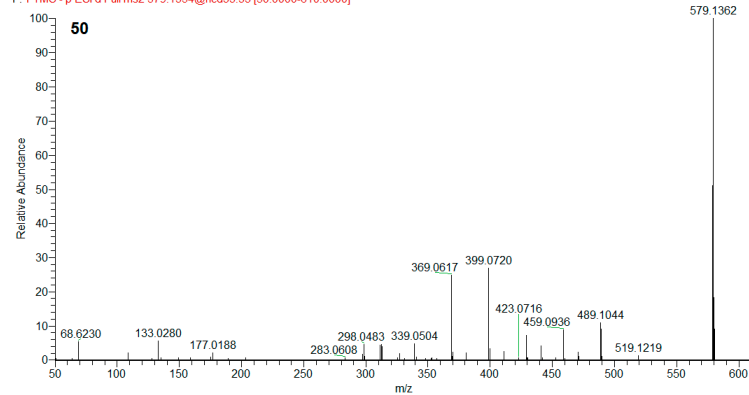
FTMS - p ESI d Full ms2 608.9992@hcd33.33 [50.0000-640.0000]



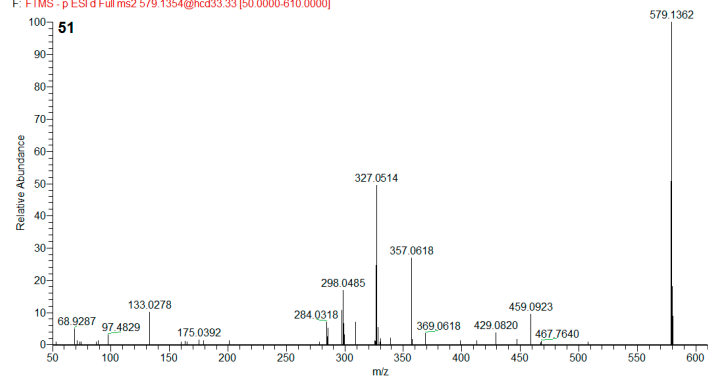
FTMS - p ESI d Full ms2 593.0060@hcd33.33 [50.0000-625.0000]



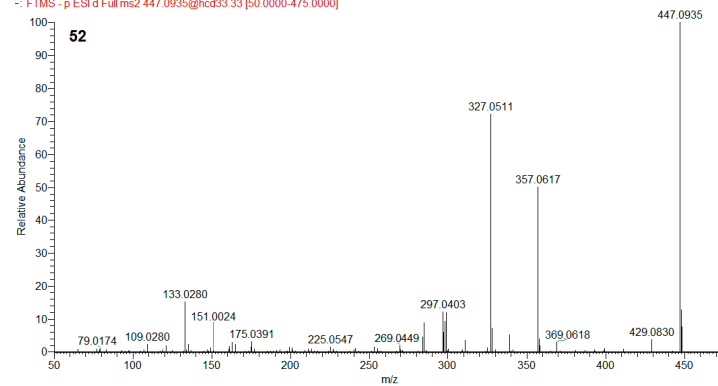
FTMS - p ESI d Full ms2 579.1354@hcd33.33 [50.0000-610.0000]



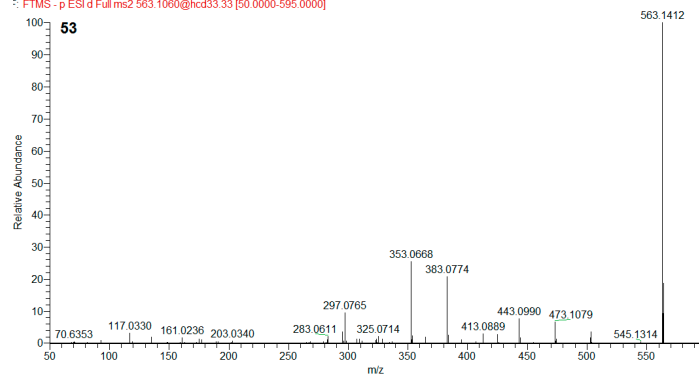
F: FTMS - p ESI'd Full ms2 579.1354@hcd33.33 [50.0000-610.0000]



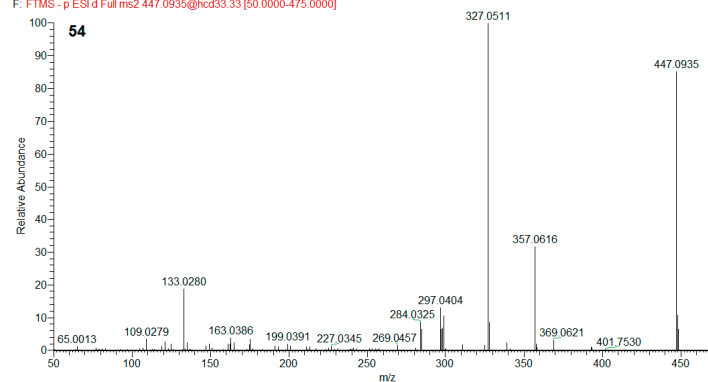
F: FTMS - p ESI'd Full ms2 447.0935@hcd33.33 [50.0000-475.0000]



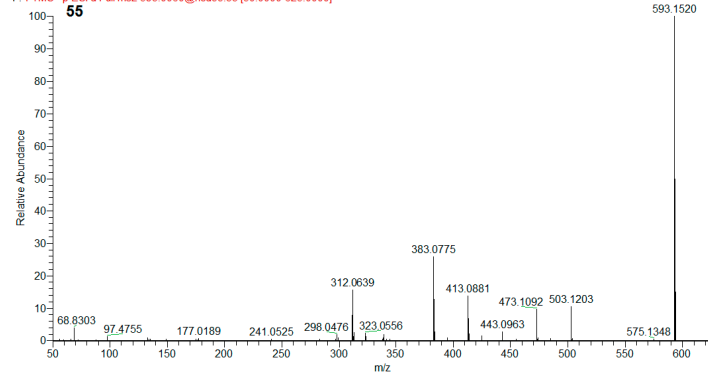
F: FTMS - p ESI'd Full ms2 563.1060@hcd33.33 [50.0000-595.0000]



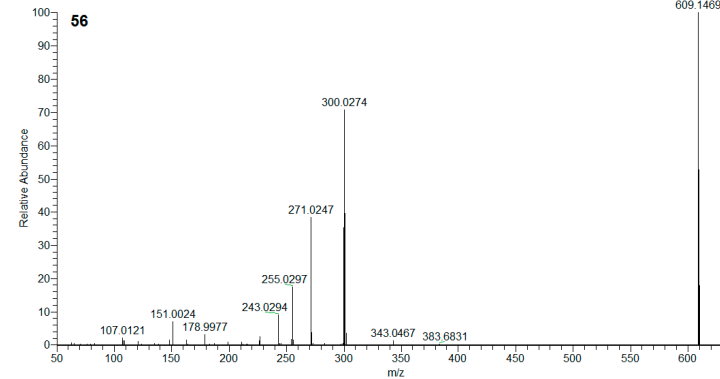
F: FTMS - p ESI'd Full ms2 447.0935@hcd33.33 [50.0000-475.0000]



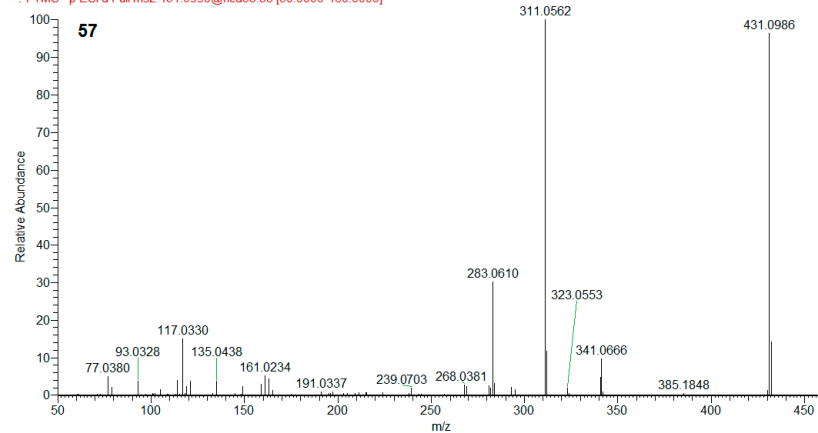
F: FTMS - p ESI d Full ms2 593.0060@hcd33.33 [50.0000-625.0000]



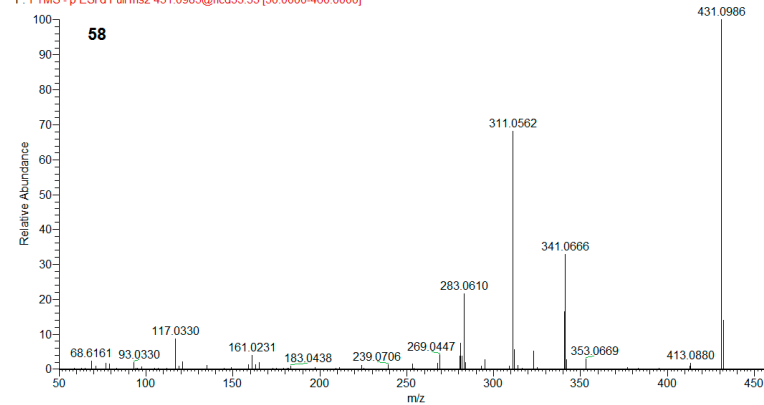
F: FTMS - p ESI d Full ms2 608.9992@hcd33.33 [50.0000-640.0000]



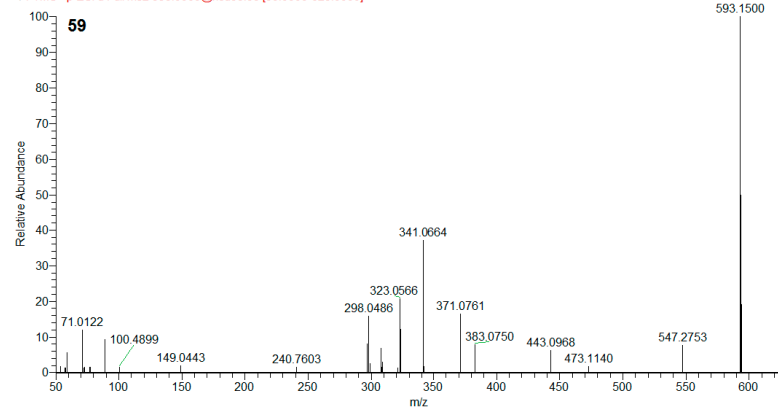
F: FTMS - p ESI d Full ms2 431.0990@hcd33.33 [50.0000-460.0000]



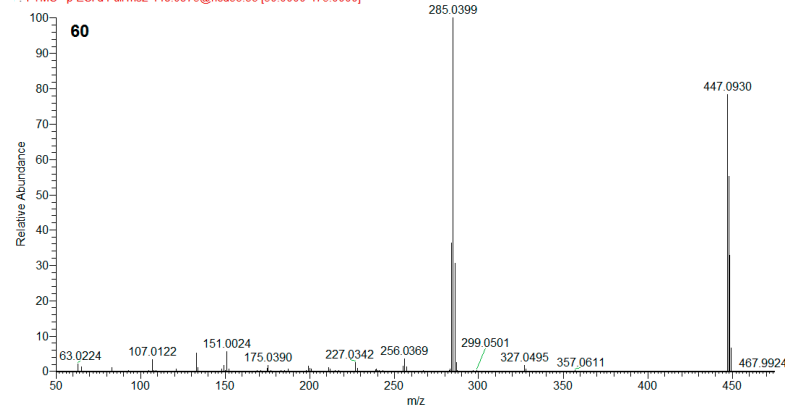
F: FTMS - p ESI d Full ms2 431.0985@hcd33.33 [50.0000-460.0000]



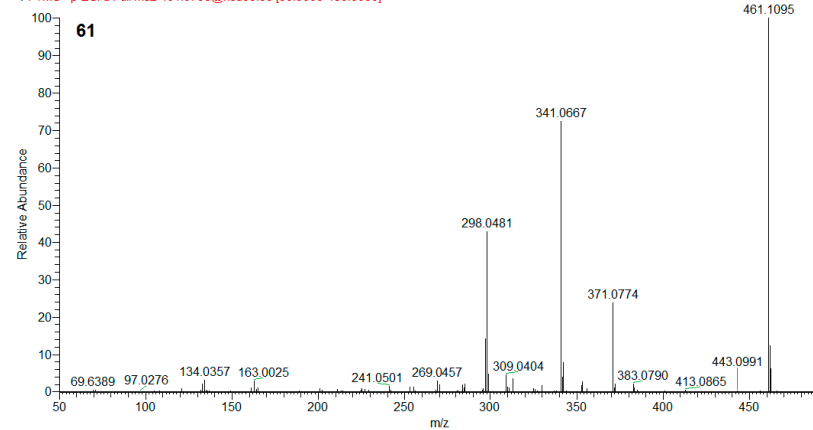
FTMS - p ESI d Full ms2 593.0060@hcd33.33 [50.0000-625.0000]



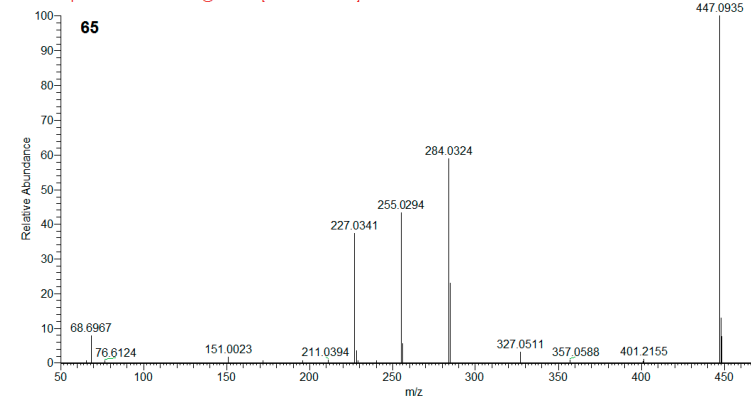
FTMS - p ESI d Full ms2 448.0975@hcd33.33 [50.0000-475.0000]



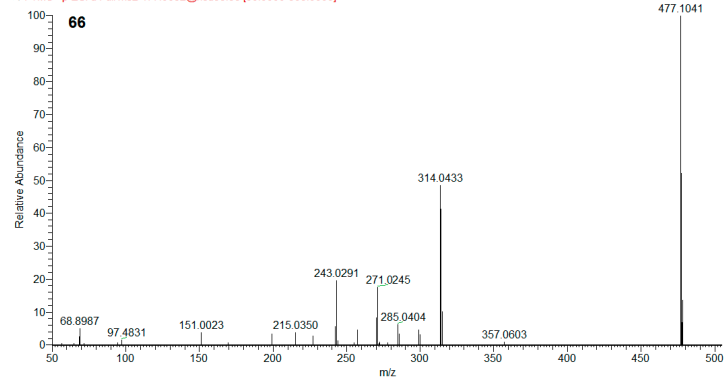
FTMS - p ESI d Full ms2 461.0735@hcd33.33 [50.0000-490.0000]



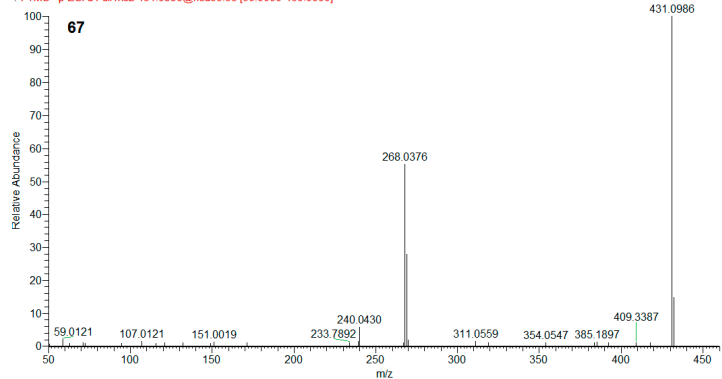
FTMS - p ESI d Full ms2 447.0935@hcd33.33 [50.0000-475.0000]



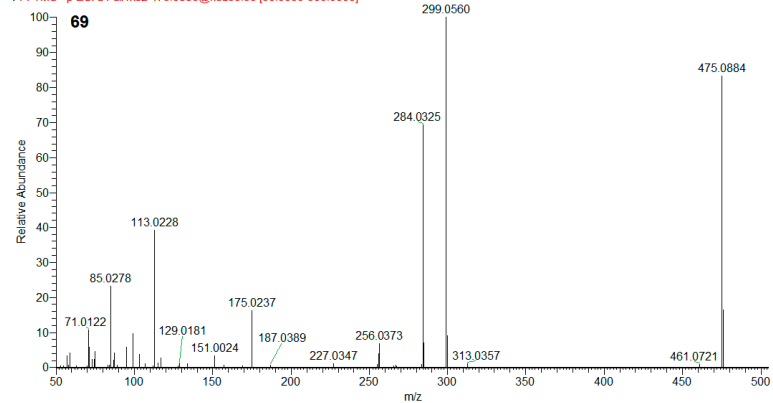
F: FTMS - p ESI<sup>-</sup> d Full ms2 477.0682@hcd33.33 [50.0000-505.0000]



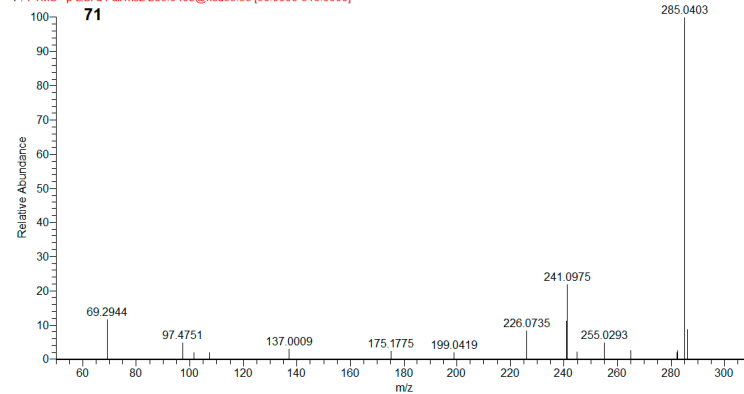
F: FTMS - p ESI<sup>-</sup> d Full ms2 431.0990@hcd33.33 [50.0000-460.0000]



F: FTMS - p ESI<sup>-</sup> d Full ms2 475.0886@hcd33.33 [50.0000-505.0000]



F: FTMS - p ESI<sup>-</sup> d Full ms2 285.0409@hcd33.33 [50.0000-310.0000]



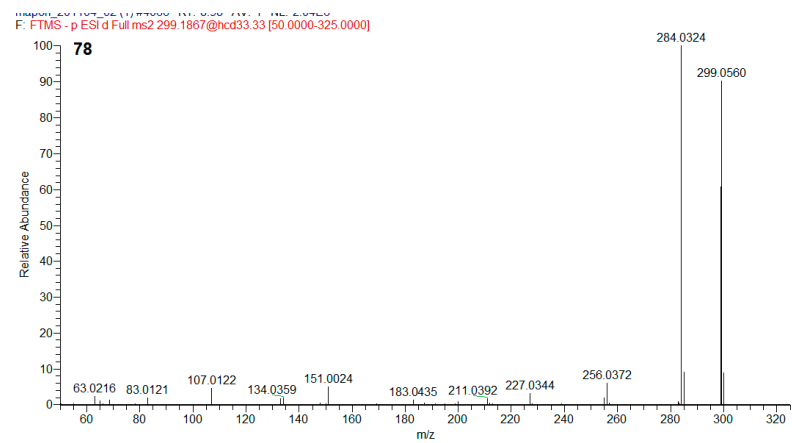
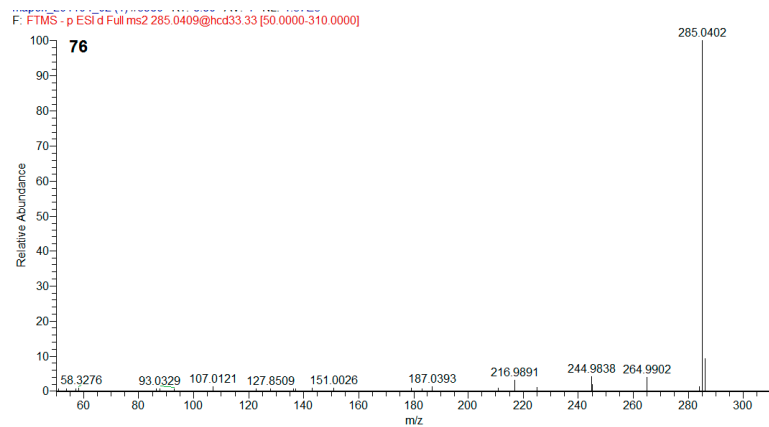
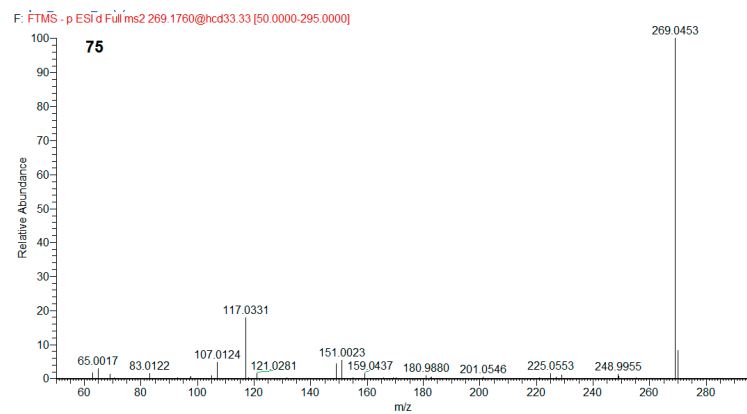
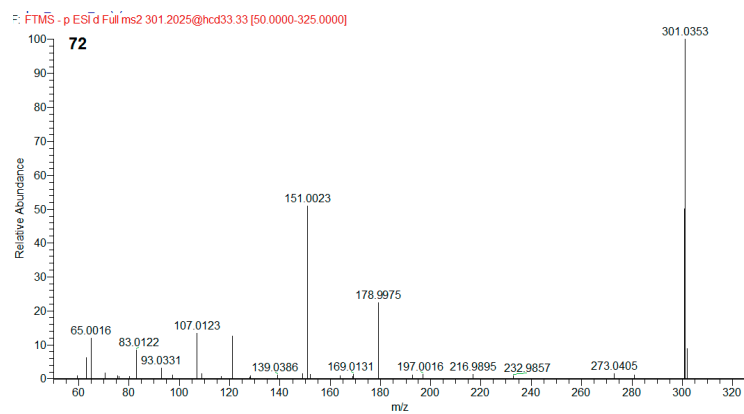
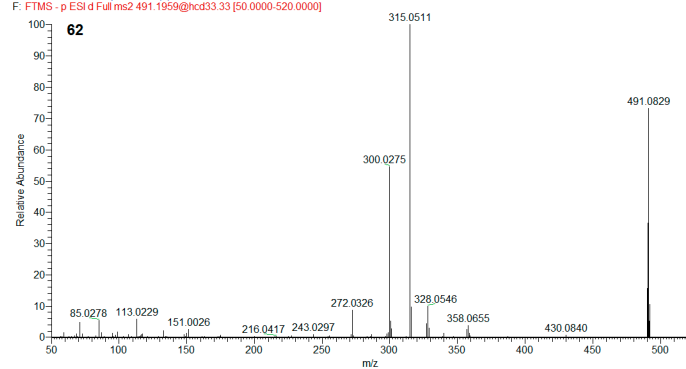
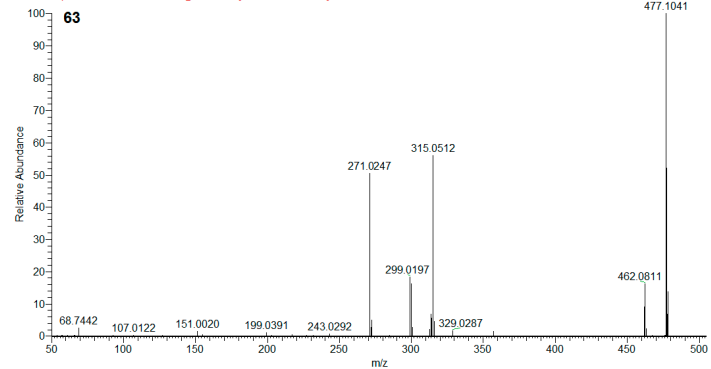


Figure S7. MS/MS spectra of C-, C,O- and O-flavonoid glycosides(for the compound numbers see Table 2).

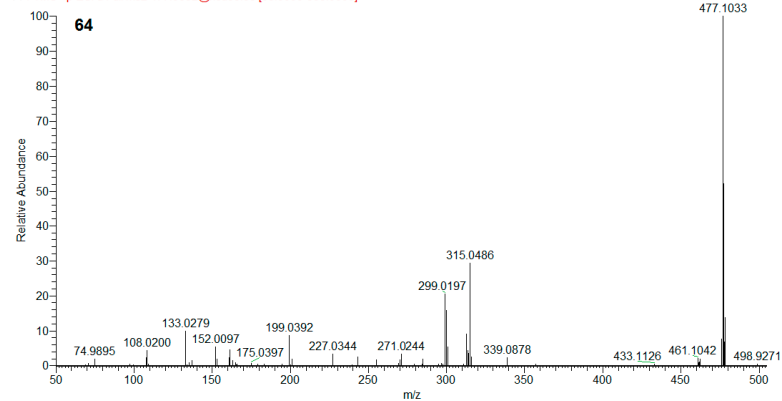
F: FTMS - p ESI d Full ms2 491.1959@hcd33.33 [50.0000-520.0000]



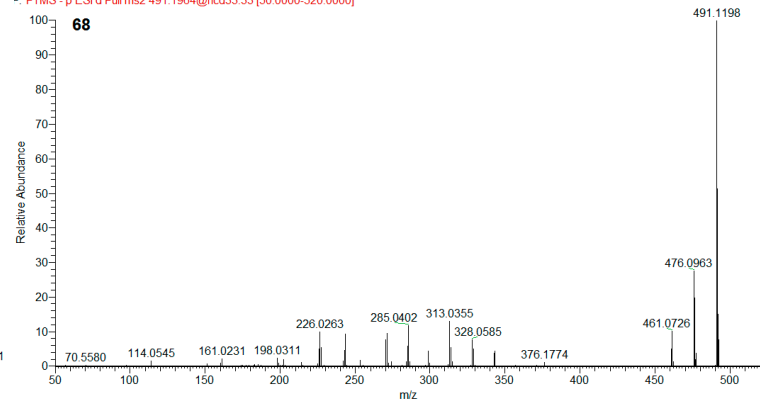
F: FTMS - p ESI d Full ms2 477.0682@hcd33.33 [50.0000-505.0000]



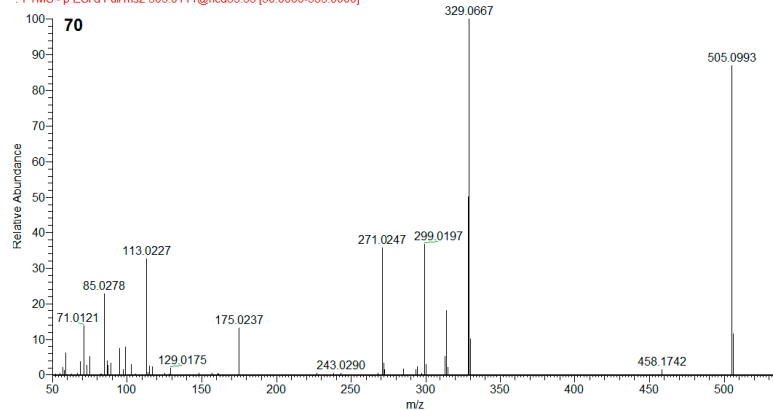
F: FTMS - p ESI d Full ms2 477.0682@hcd33.33 [50.0000-505.0000]



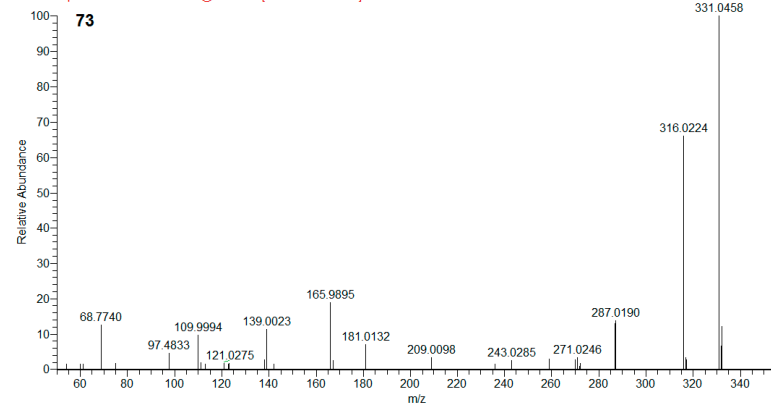
F: FTMS - p ESI d Full ms2 491.1964@hcd33.33 [50.0000-520.0000]



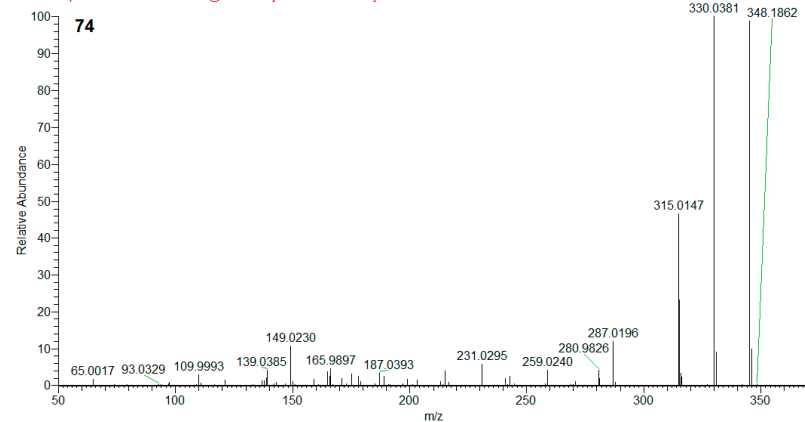
F: FTMS - p ESI d Full ms2 505.0111@hcd33.33 [50.0000-535.0000]



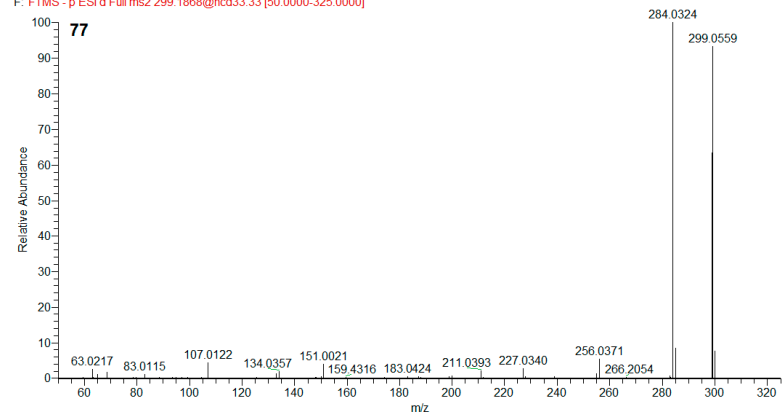
F: FTMS - p ESI d Full ms2 331.2048@hcd33.33 [50.0000-355.0000]



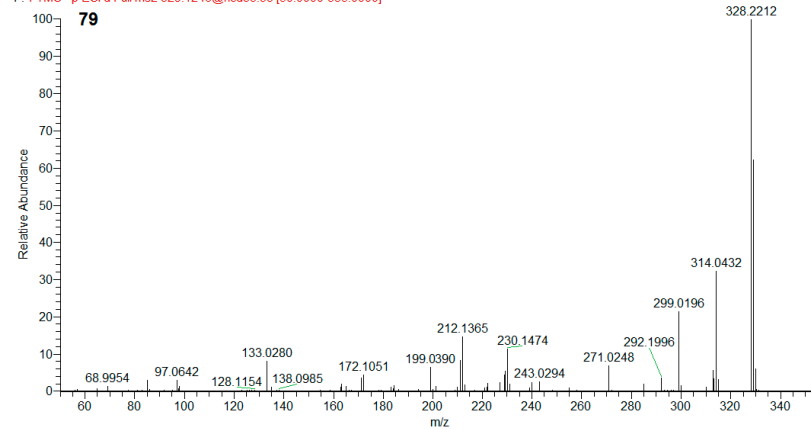
F: FTMS - p ESI d Full ms2 345.1840@hcd33.33 [50.0000-370.0000]



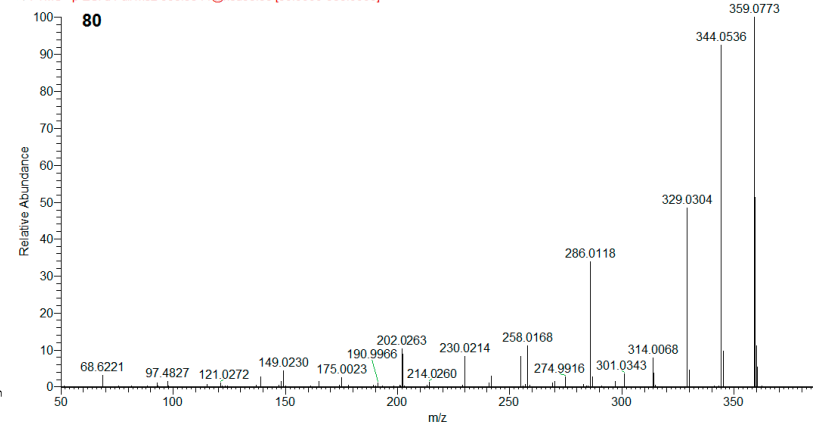
F: FTMS - p ESI d Full ms2 299.1868@hcd33.33 [50.0000-325.0000]



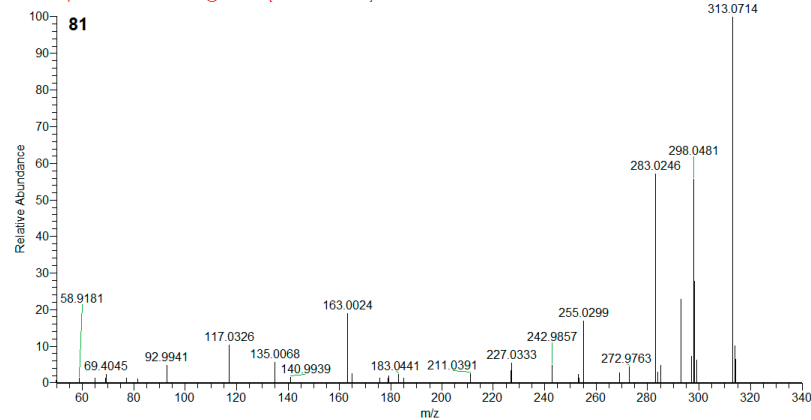
F: FTMS - p ESI d Full ms2 329.1246@hcd33.33 [50.0000-355.0000]



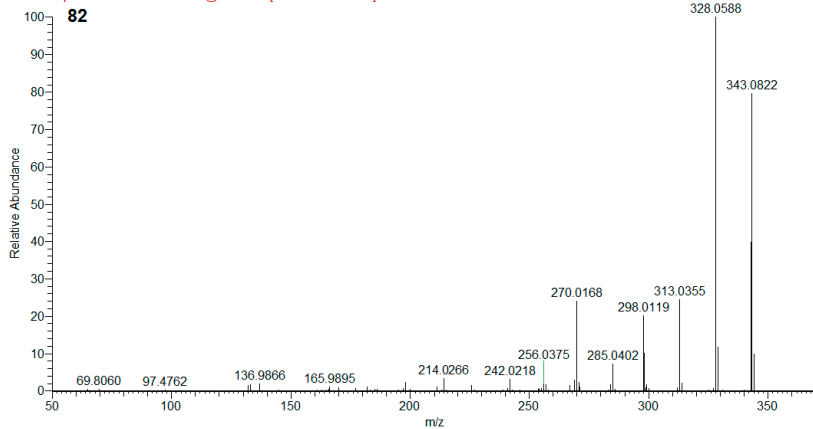
F: FTMS - p ESI d Full ms2 358.9944@hcd33.33 [50.0000-385.0000]



F: FTMS - p ESI d Full ms2 313.0569@hcd33.33 [50.0000-340.0000]



F: FTMS - p ESI d Full ms2 343.0001@hcd33.33 [50.0000-370.0000]



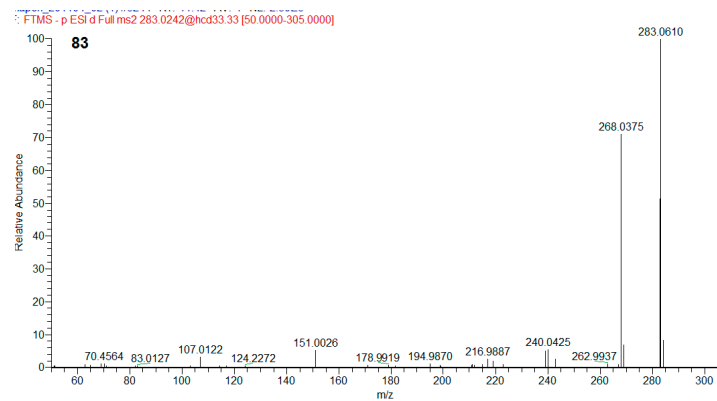
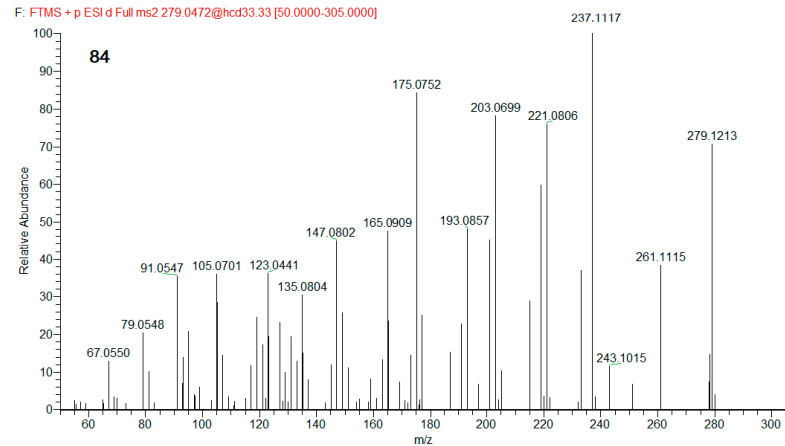
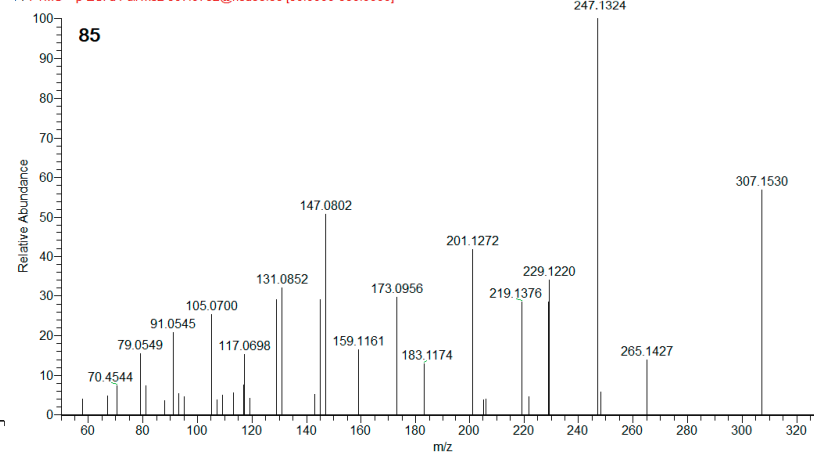


Figure S8. MS/MS spectra of 6-methoxyflavonoids (aglycones and glycosides) (for the compound numbers see Table 2).

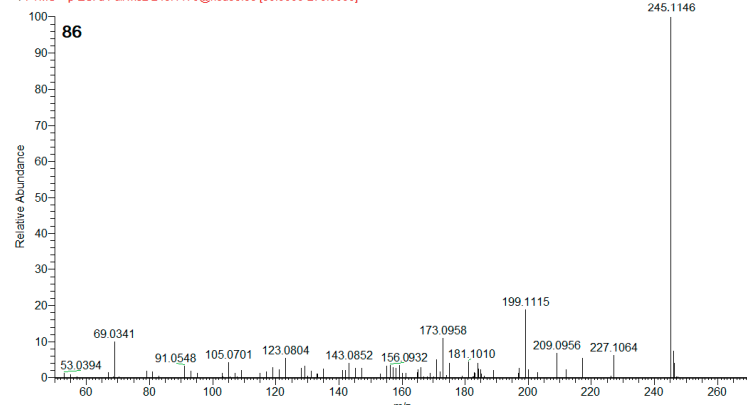
F: FTMS + p ESI d Full ms2 279.0472@hcd33.33 [50.0000-305.0000]



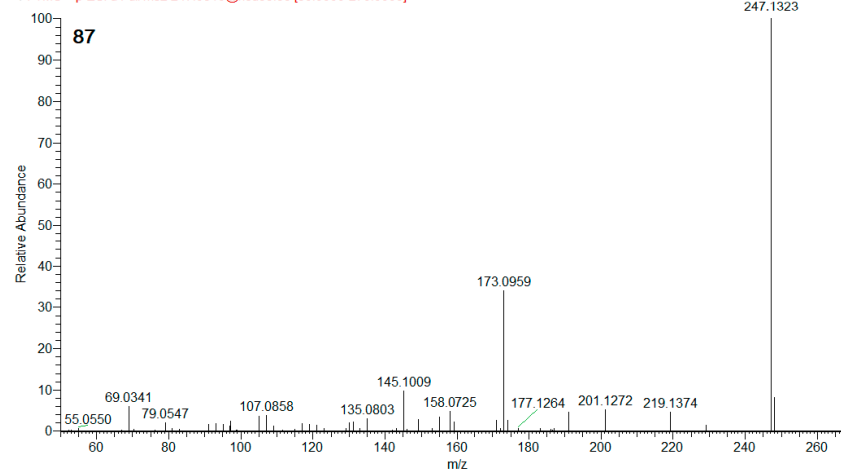
F: FTMS + p ESI d Full ms2 307.0782@hcd33.33 [50.0000-330.0000]



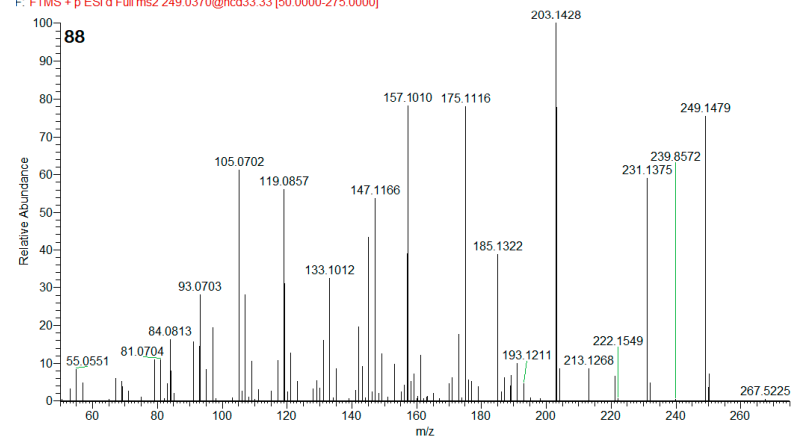
F: FTMS + p ESI d Full ms2 245.1170@hcd33.33 [50.0000-270.0000]



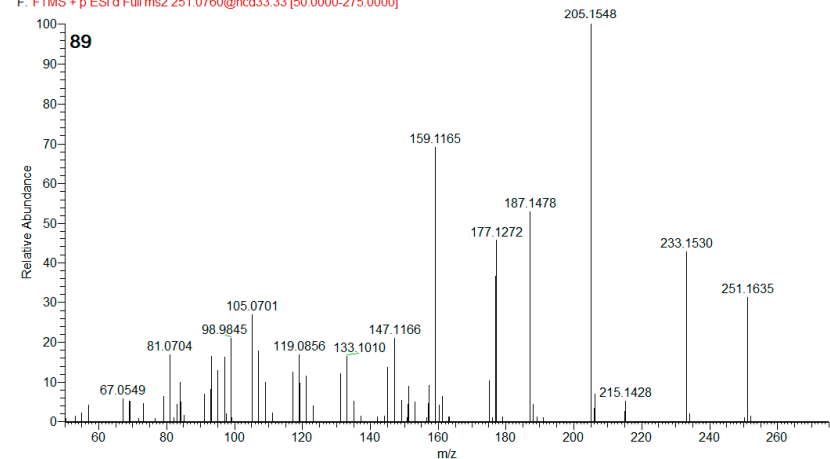
F: FTMS + p ESI d Full ms2 247.0810@hcd33.33 [50.0000-270.0000]



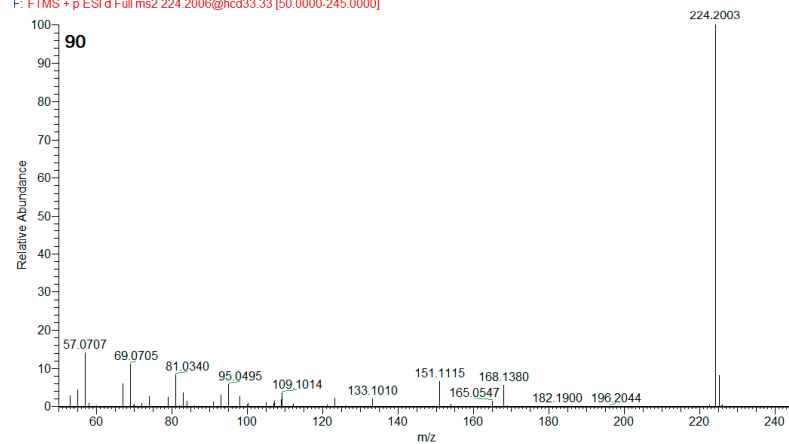
F: FTMS + p ESI d Full ms2 249.0370@hcd33.33 [50.0000-275.0000]



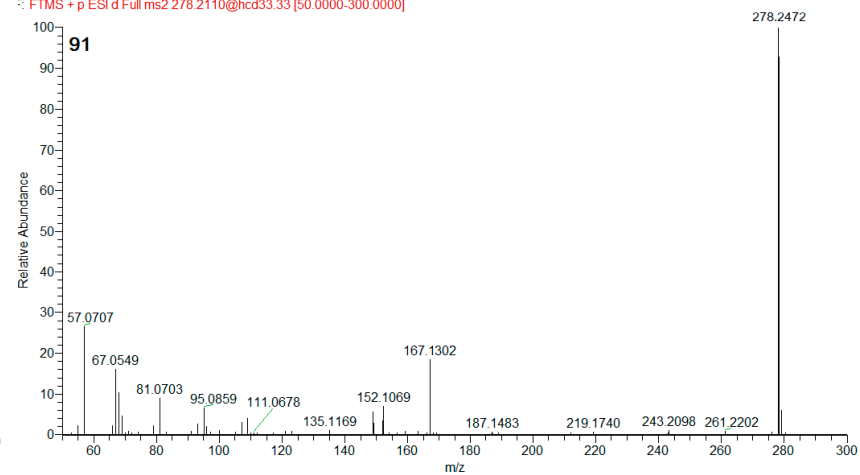
F: FTMS + p ESI d Full ms2 251.0760@hcd33.33 [50.0000-275.0000]



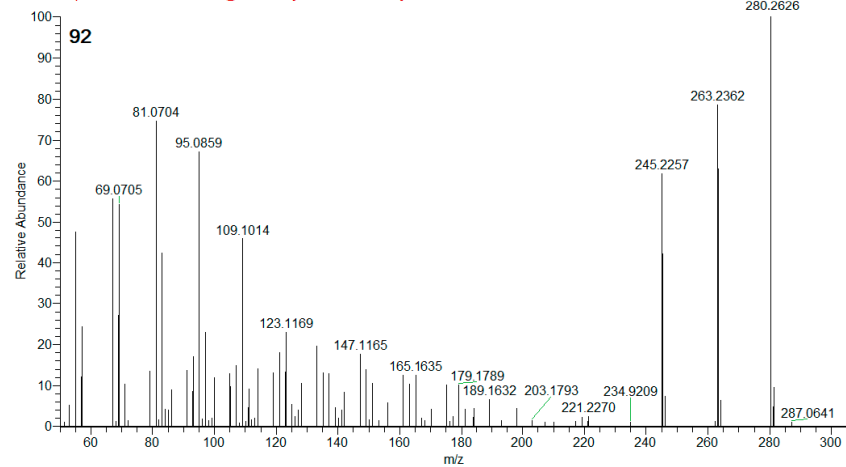
F: FTMS + p ESI d Full ms2 224.2006@hcd33.33 [50.0000-245.0000]



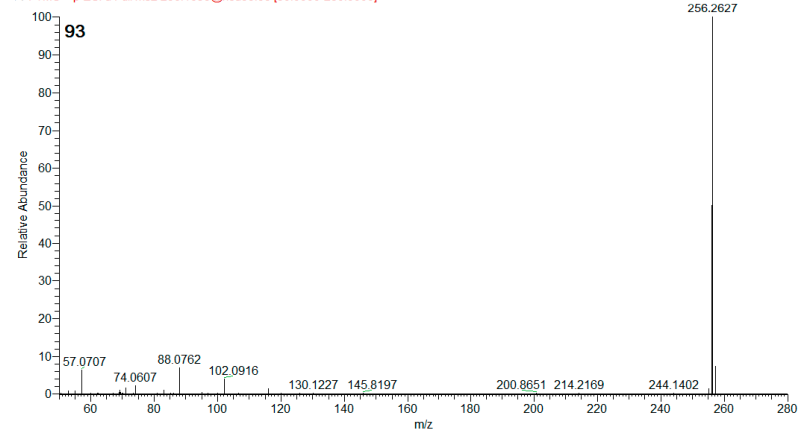
F: FTMS + p ESI d Full ms2 278.2110@hcd33.33 [50.0000-300.0000]



FTMS + p ESI d Full ms2 280.1905@hcd33.33 [50.0000-305.0000]



FTMS + p ESI d Full ms2 256.1693@hcd33.33 [50.0000-280.0000]



FTMS + p ESI d Full ms2 282.0784@hcd33.33 [50.0000-305.0000]

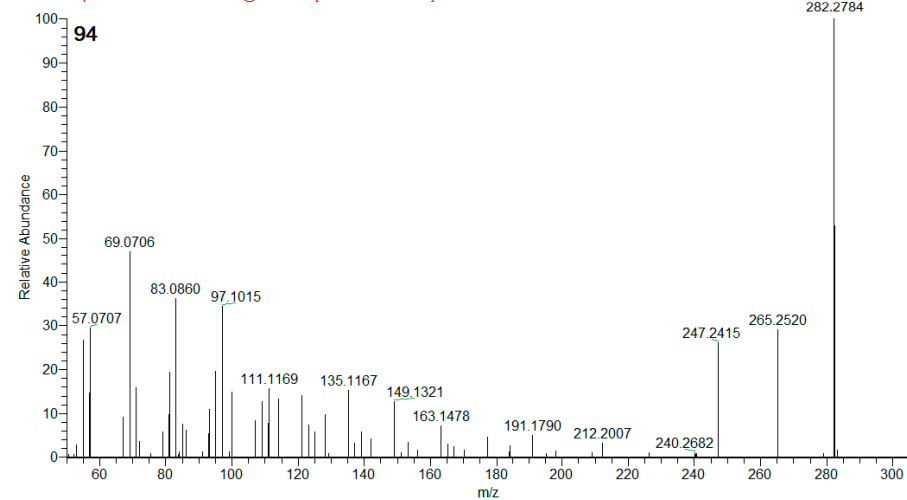


Figure S9. MS/MS spectra of sesquiterpene lactones (for the compound numbers see Table 2).

