Supplementary Material

Anti-obesity Effects of Secondary Metabolites from *Chrysosplenium flagelliferum*: *In Vitro* and *In Silico* Studies

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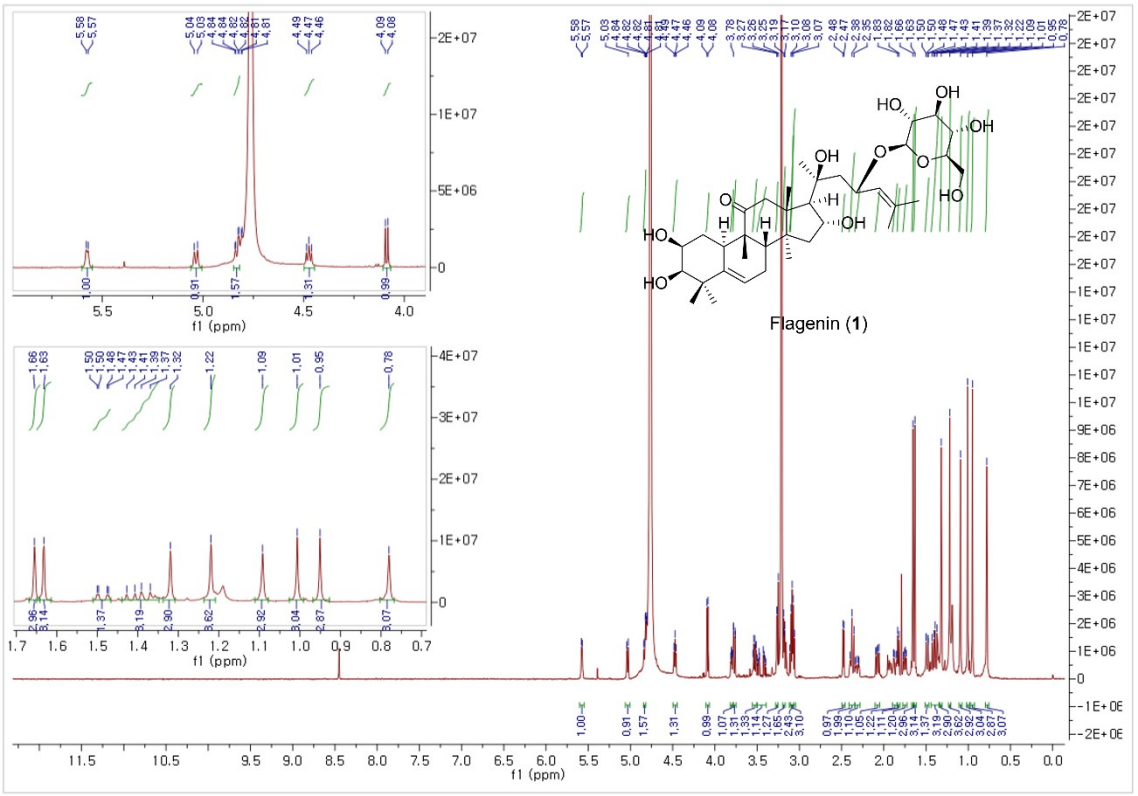


Figure S1. ^{1}H NMR spectrum (850 MHz, CD_3OD) of compound **1**

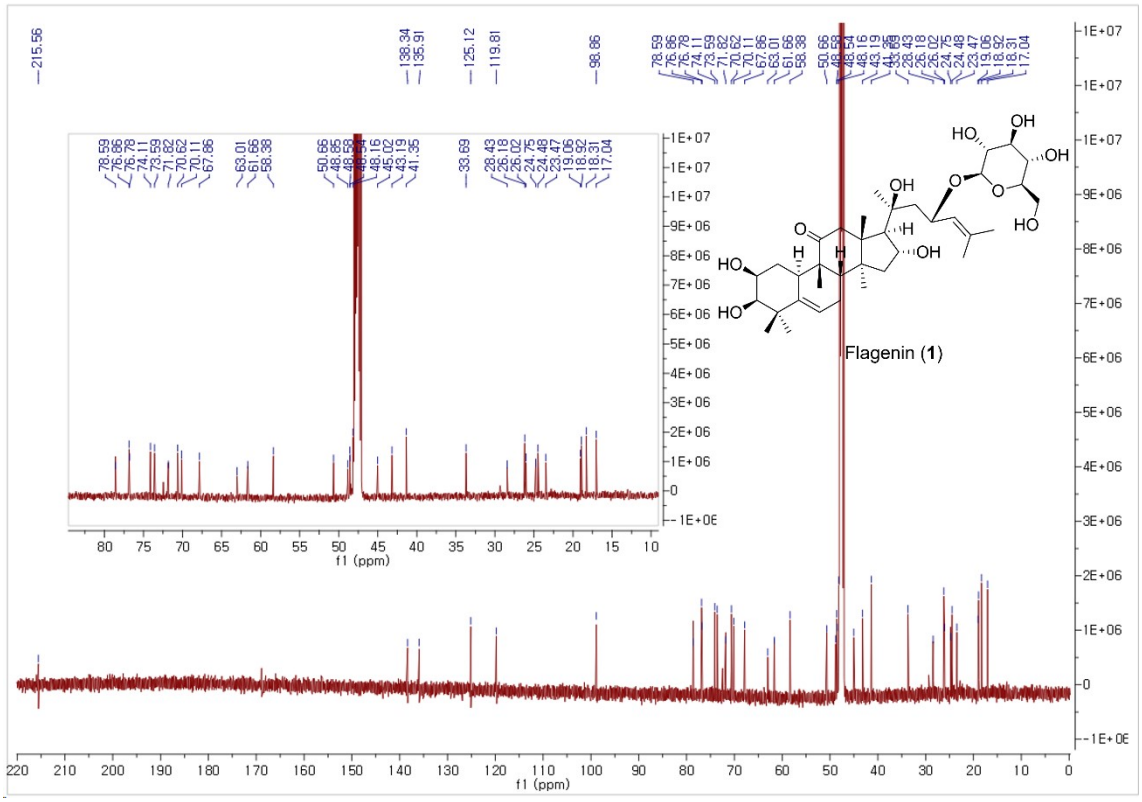


Figure S2. ^{13}C NMR spectrum (212.5 MHz, CD_3OD) of compound **1**

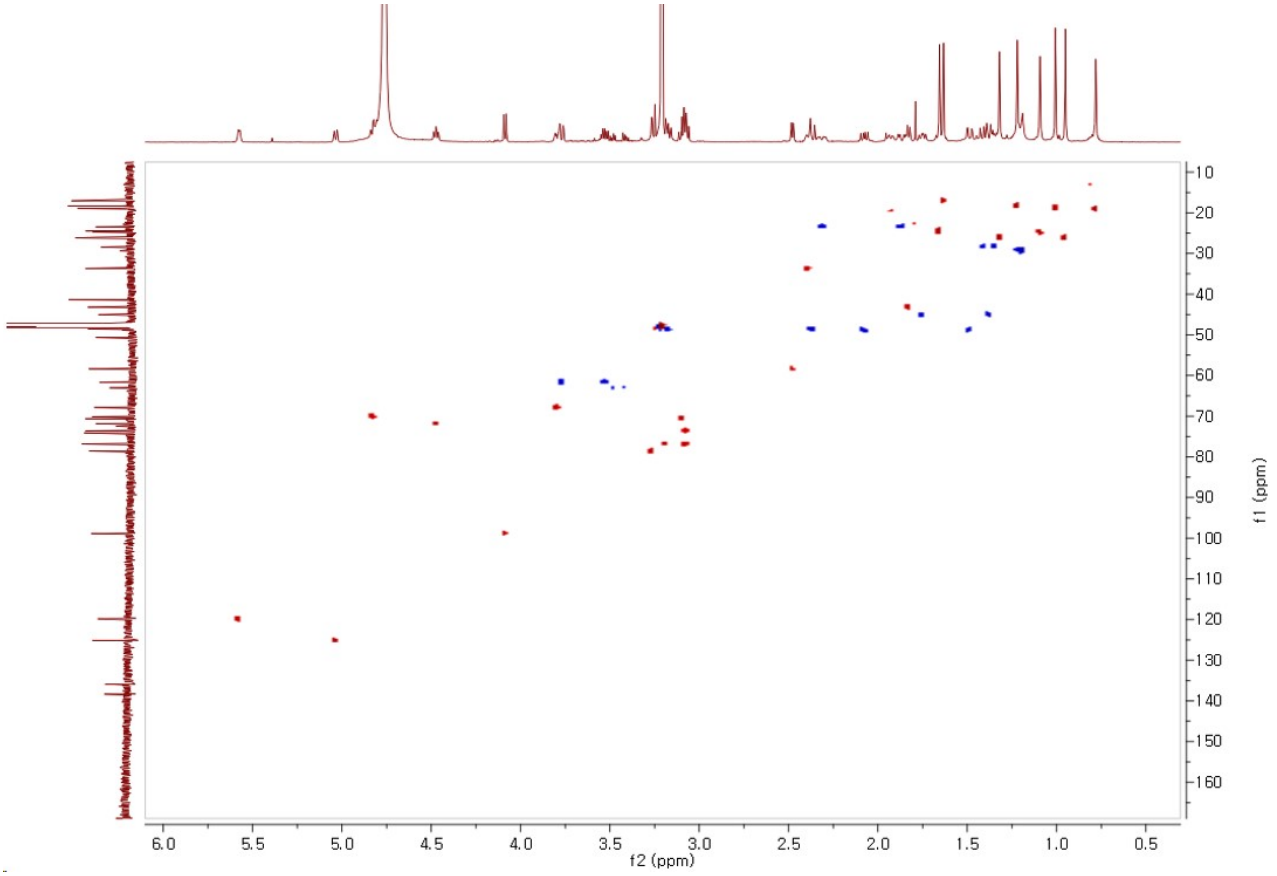


Figure S3. HSQC spectrum of compound **1**

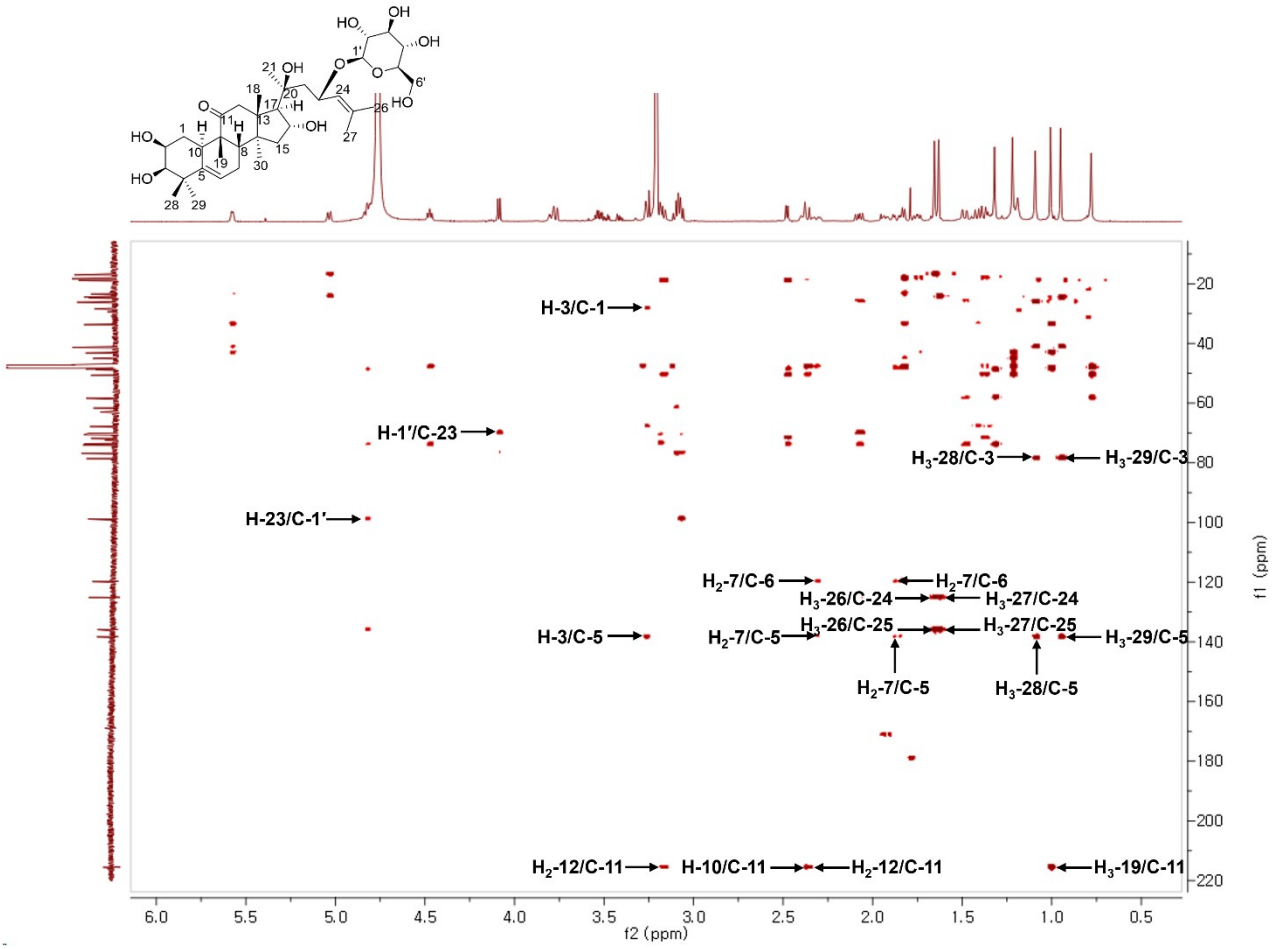


Figure S4. HMBC spectrum of compound **1**

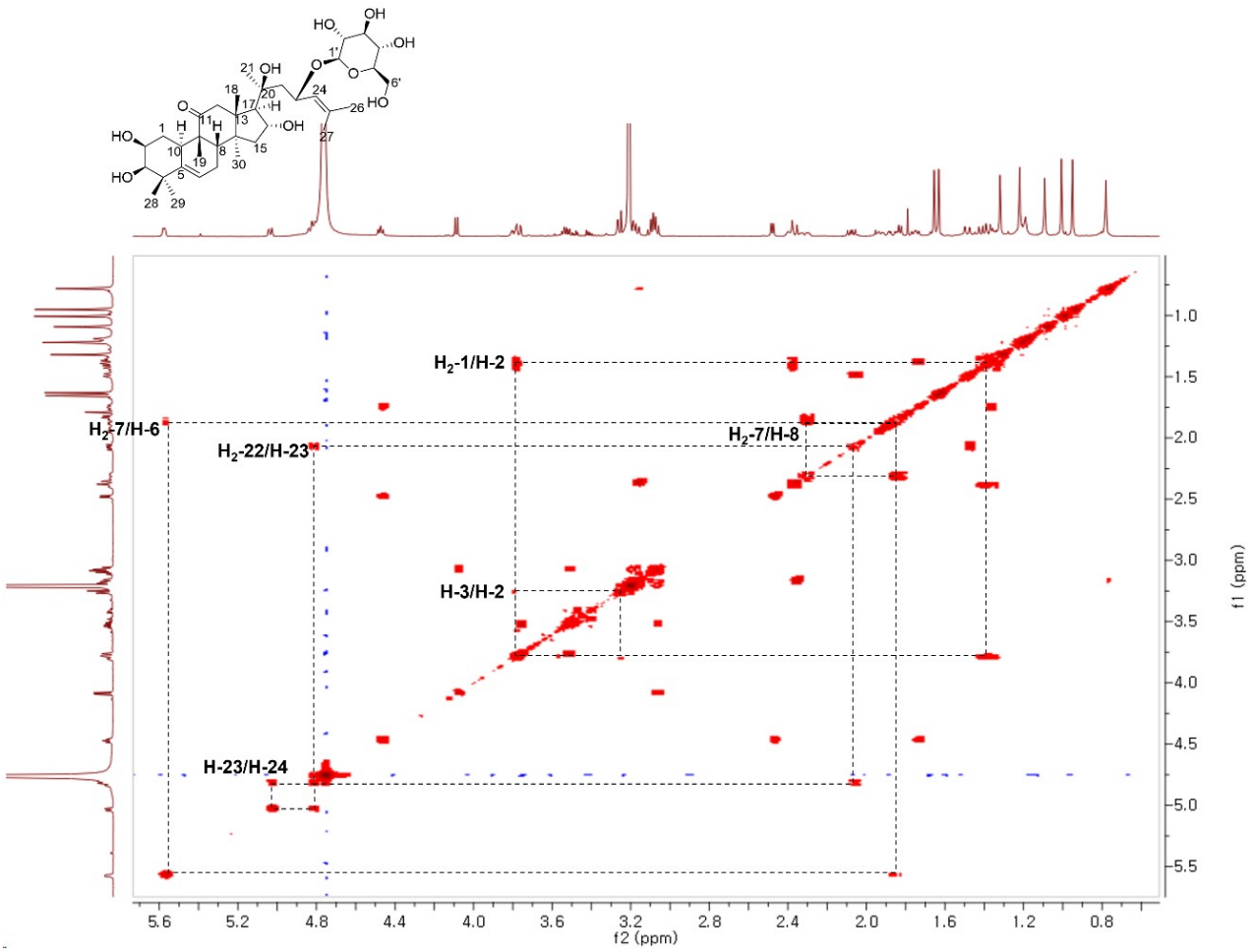


Figure S5. ^{1}H-^{1}H COSY spectrum of compound **1**

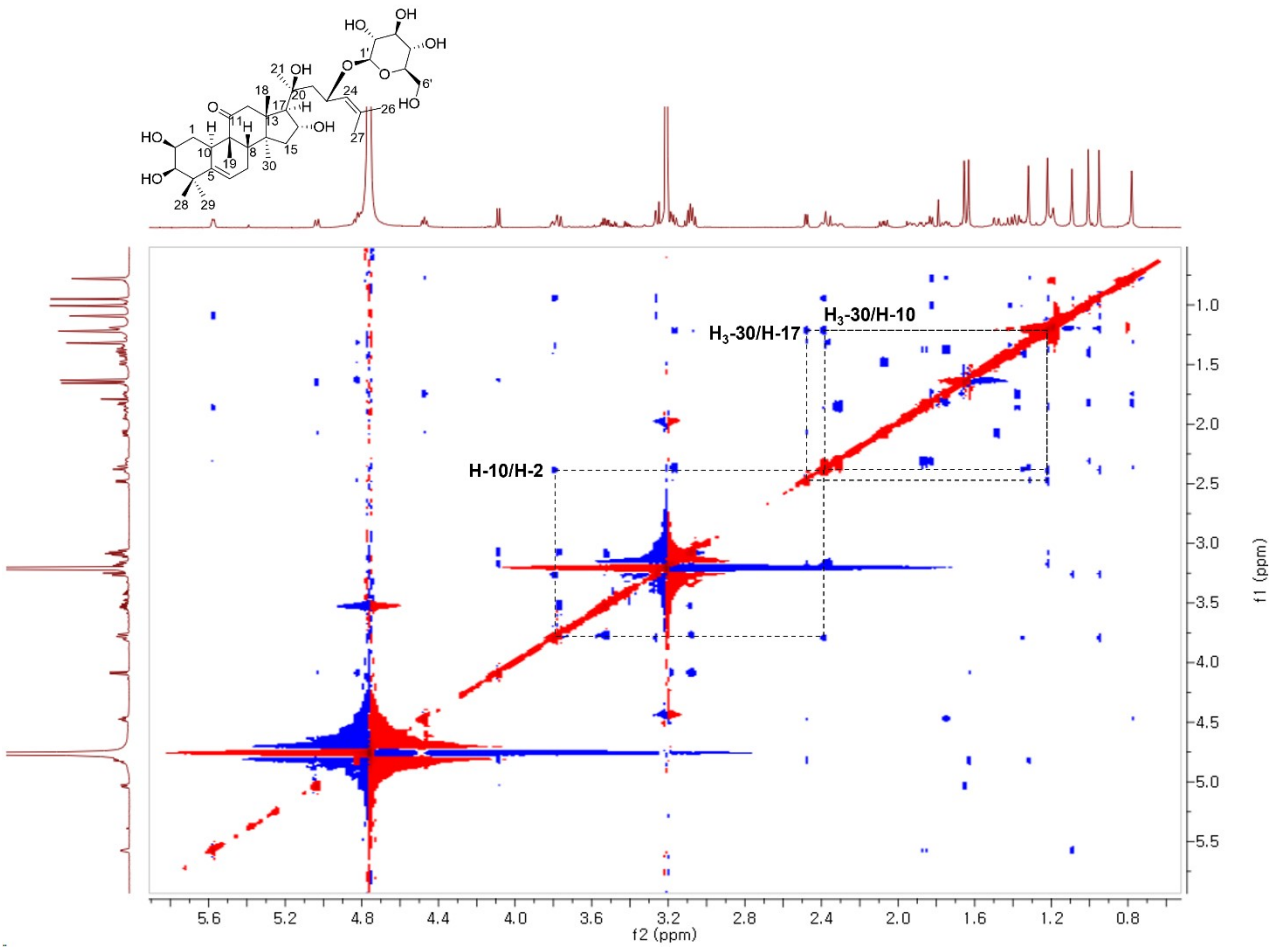


Figure S6. ROESY spectrum of compound **1**

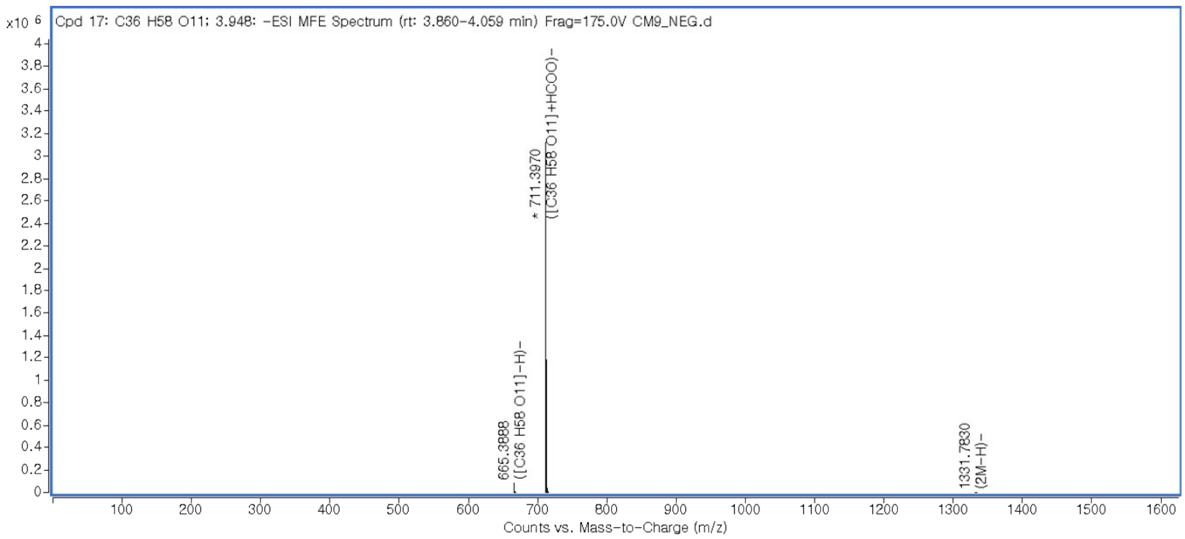


Figure S7. HR-ESI-MS spectrum of compound **1**

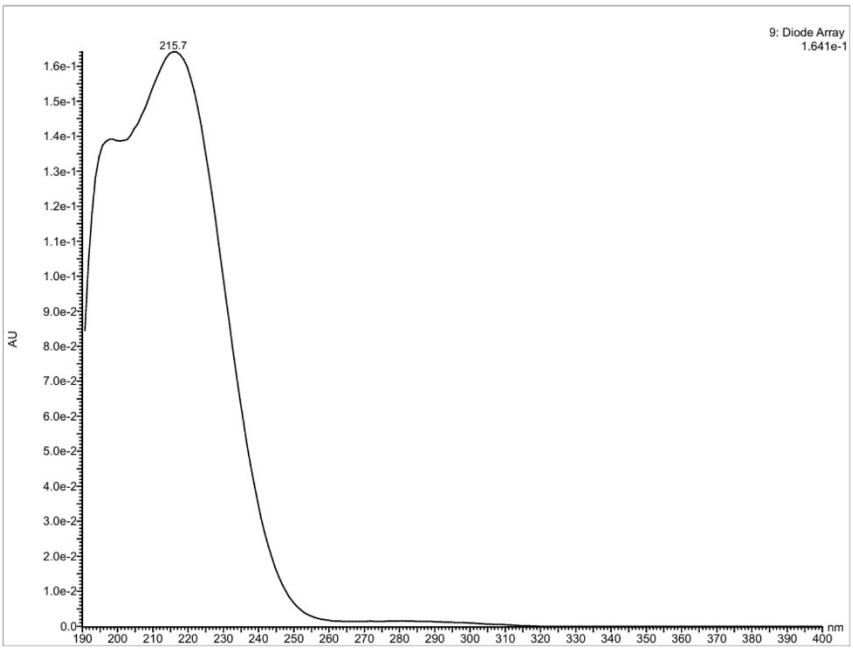


Figure S8. UV spectrum of compound **1**

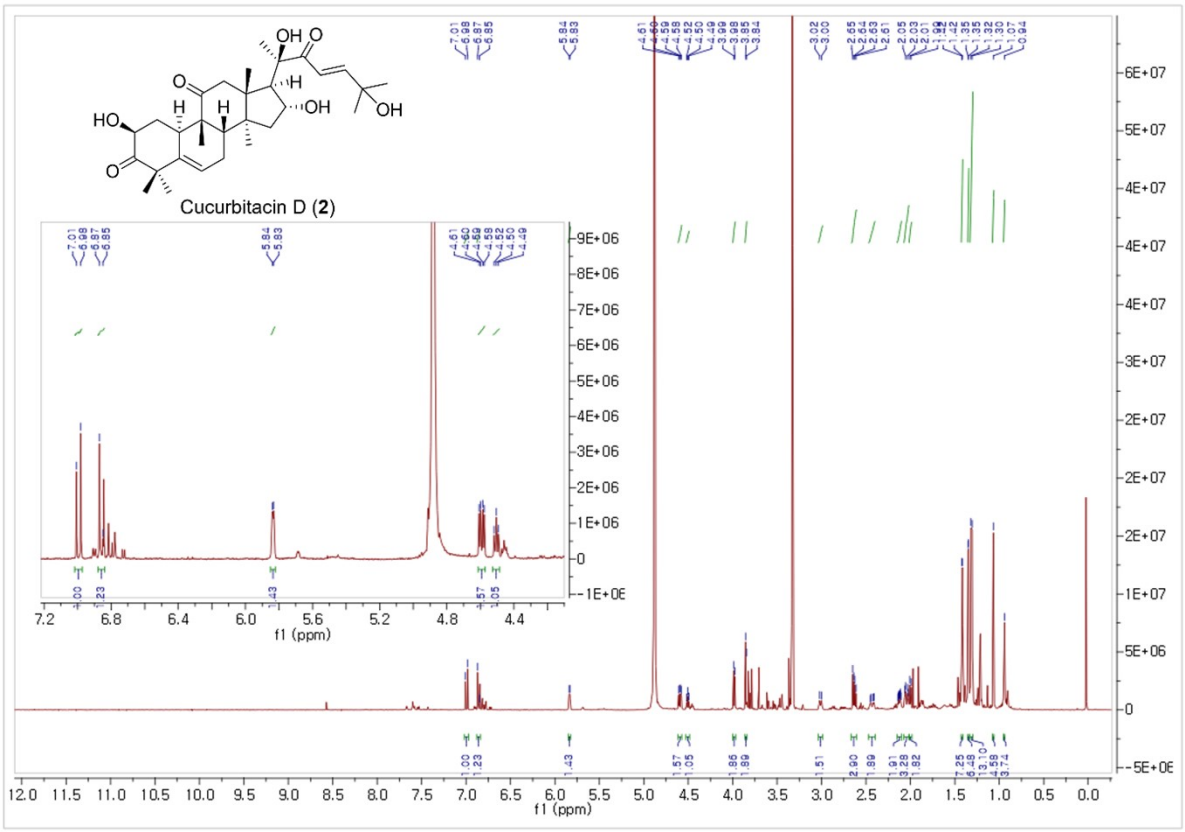


Figure S9. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **2**

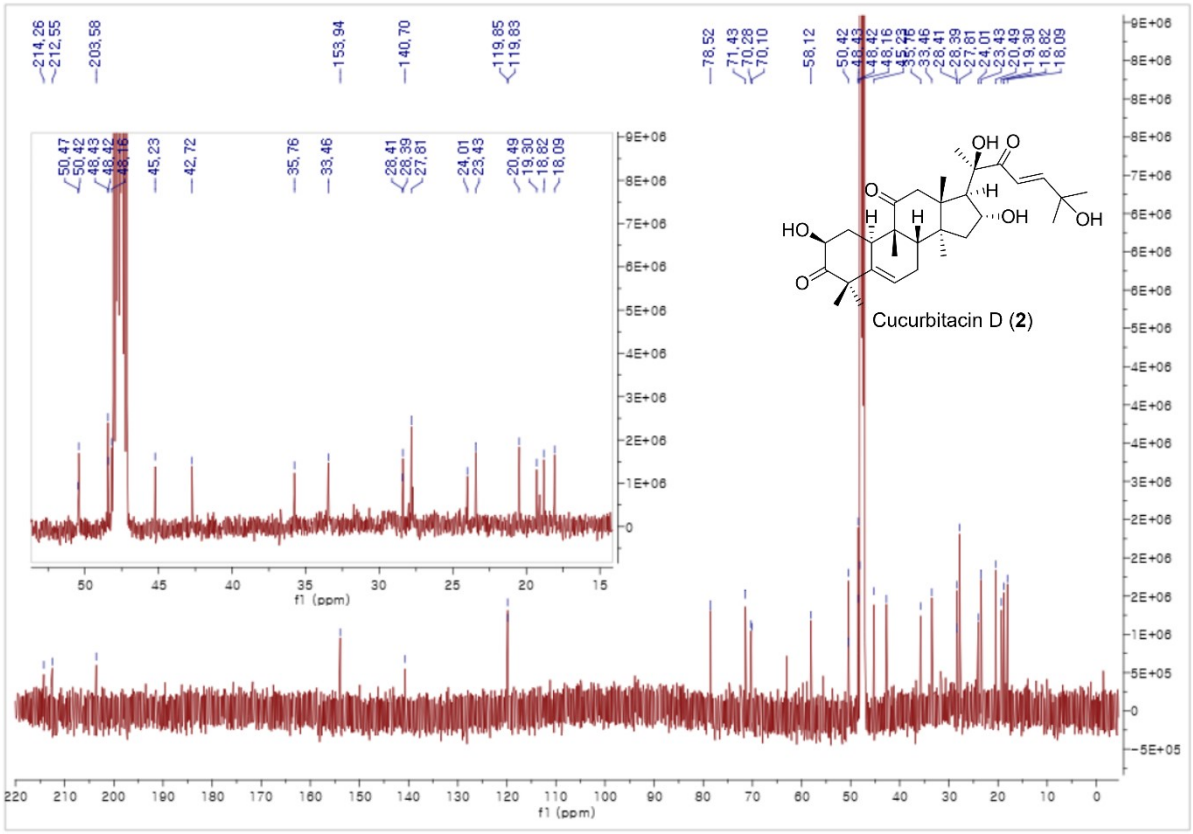


Figure S10. ^{13}C NMR spectrum (150 MHz, $CDCl_3$) of compound **2**

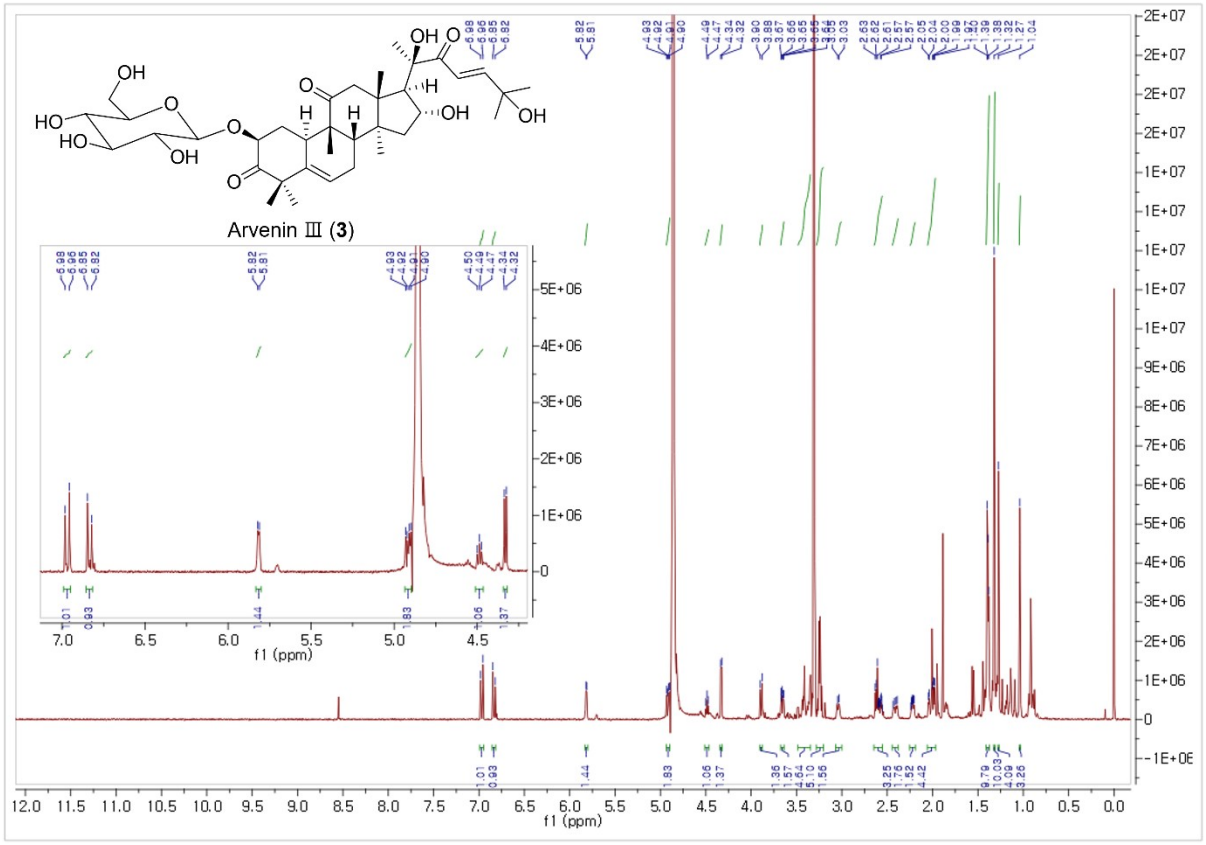


Figure S11. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **3**

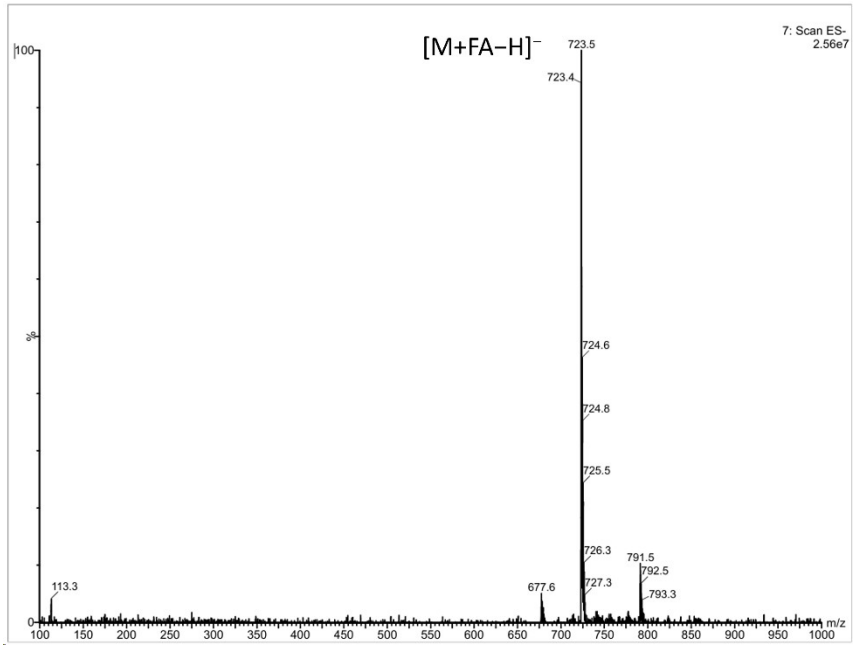


Figure S12. ESI-MS spectrum of compound **3**

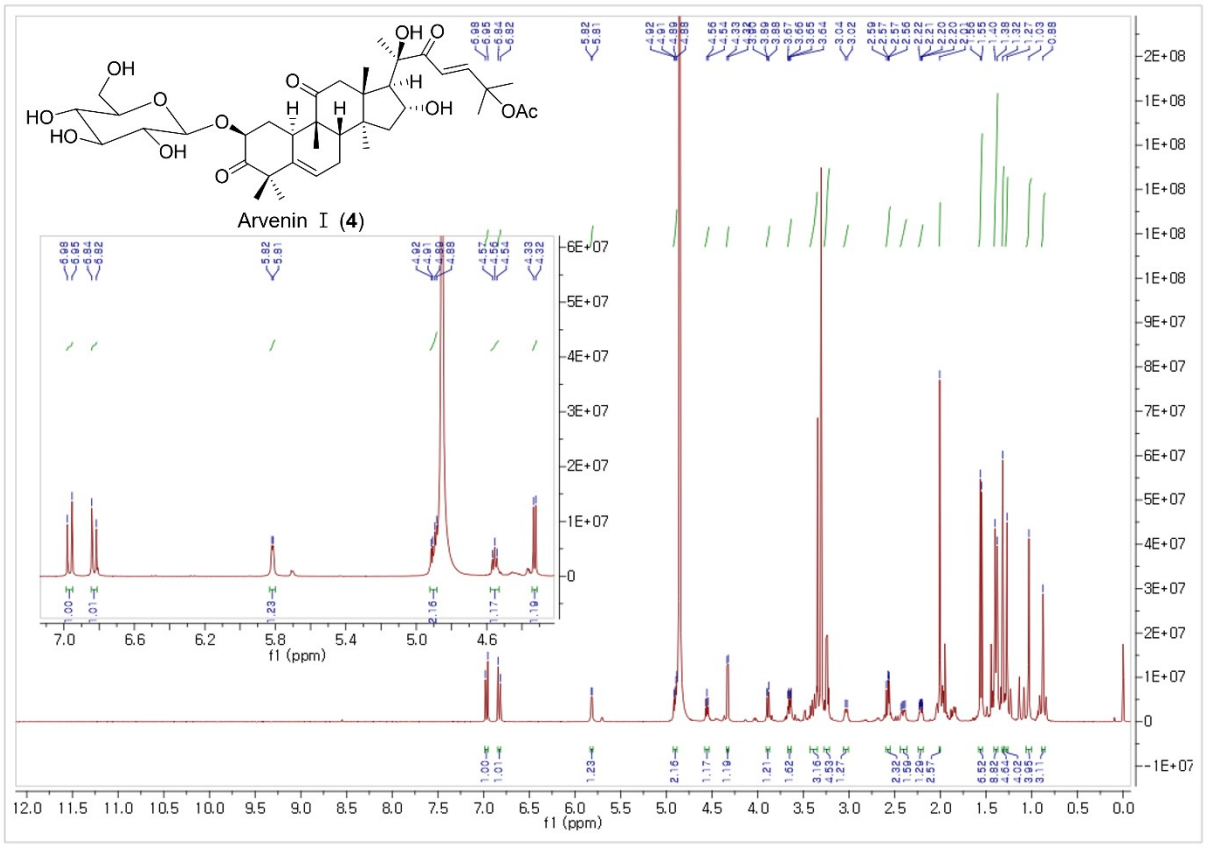


Figure S13. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **4**

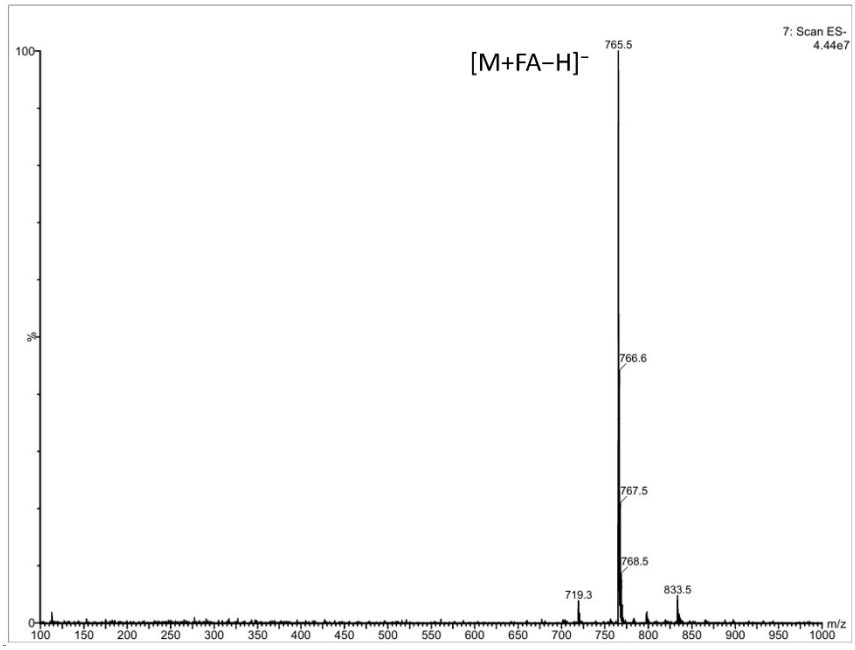


Figure S14. ESI-MS spectrum of compound **4**

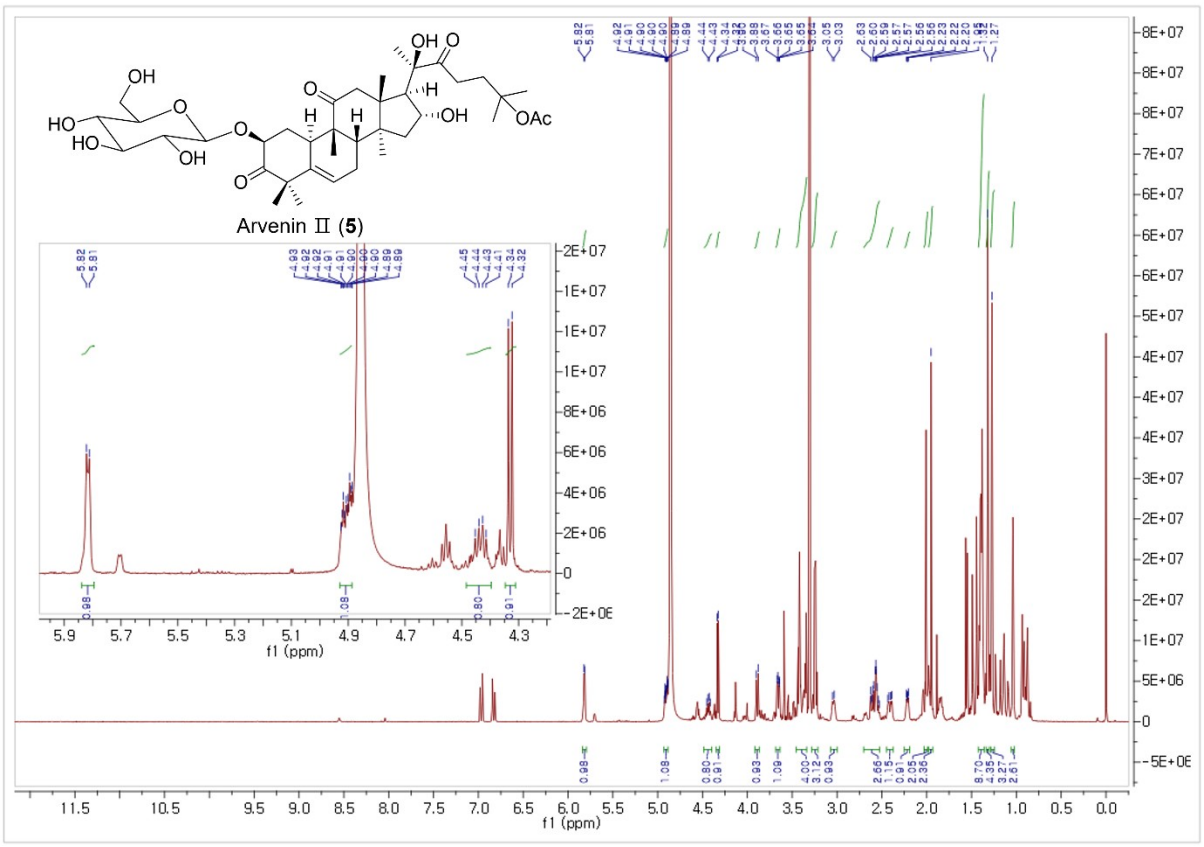


Figure S15. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **5**

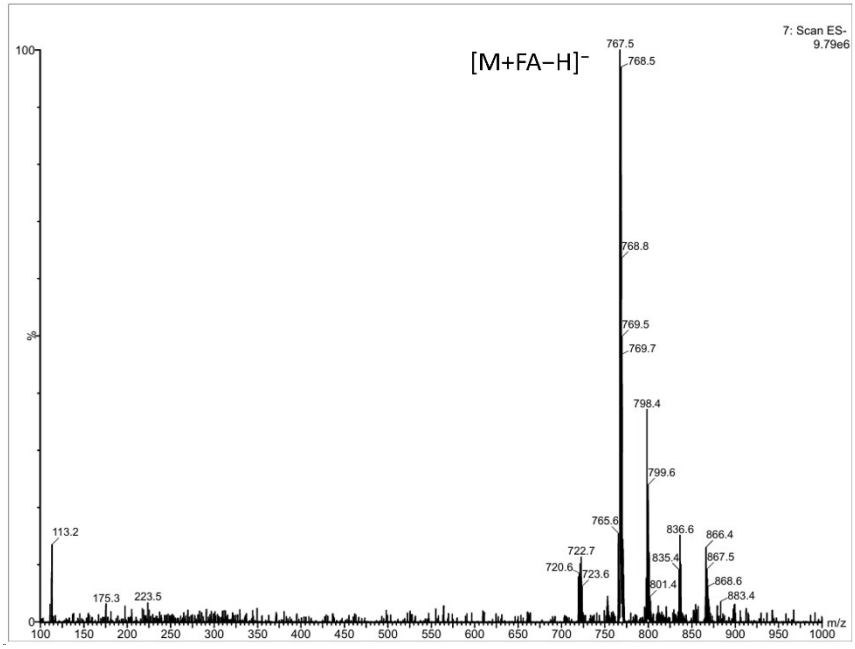


Figure S16. ESI-MS spectrum of compound **5**

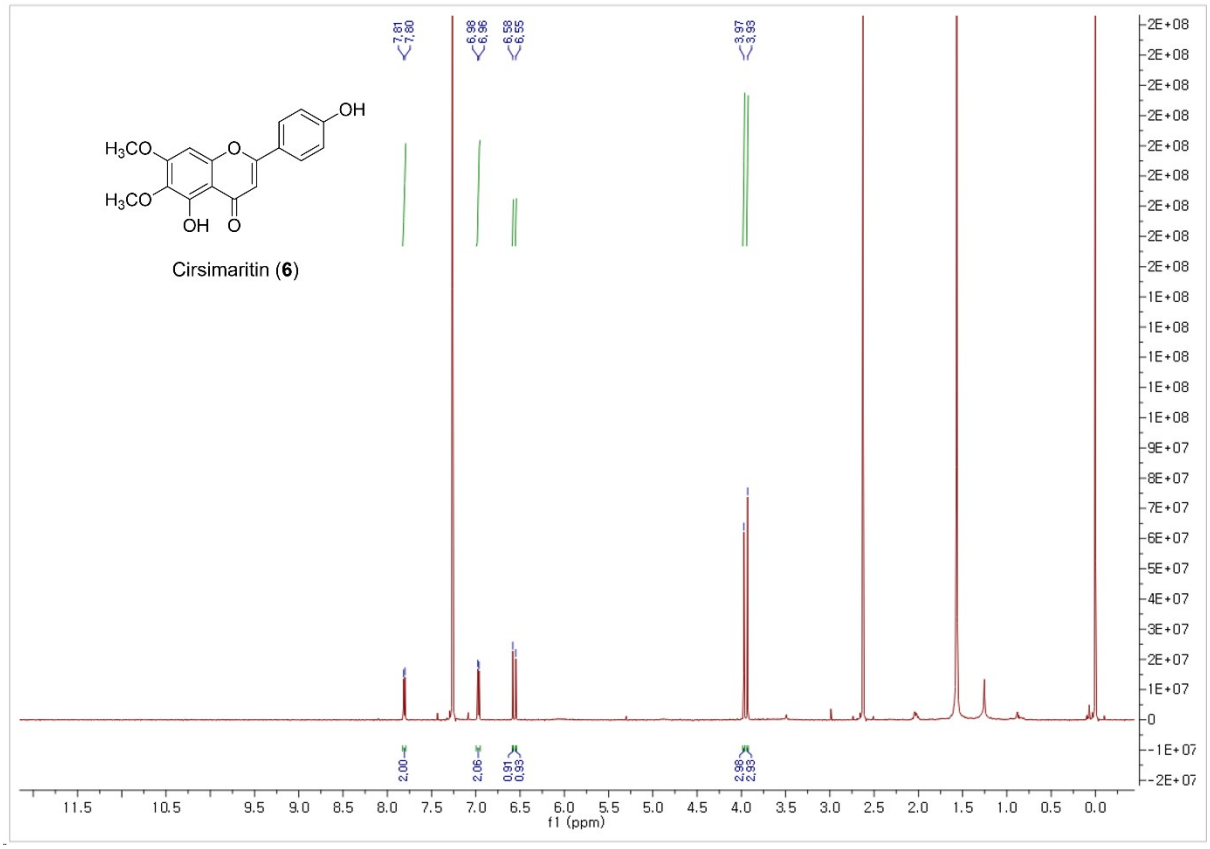


Figure S17. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **6**

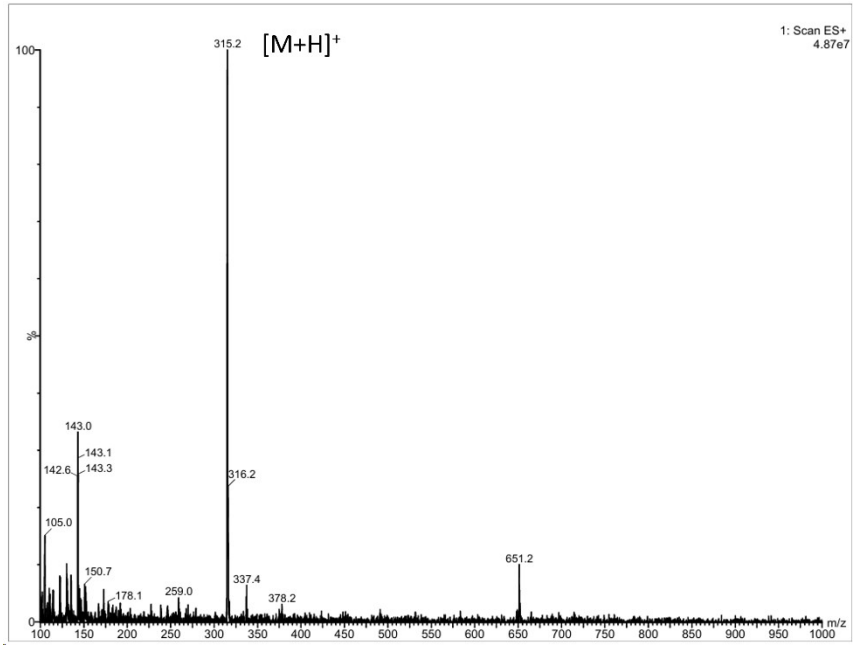


Figure S18. ESI-MS spectrum of compound **6**

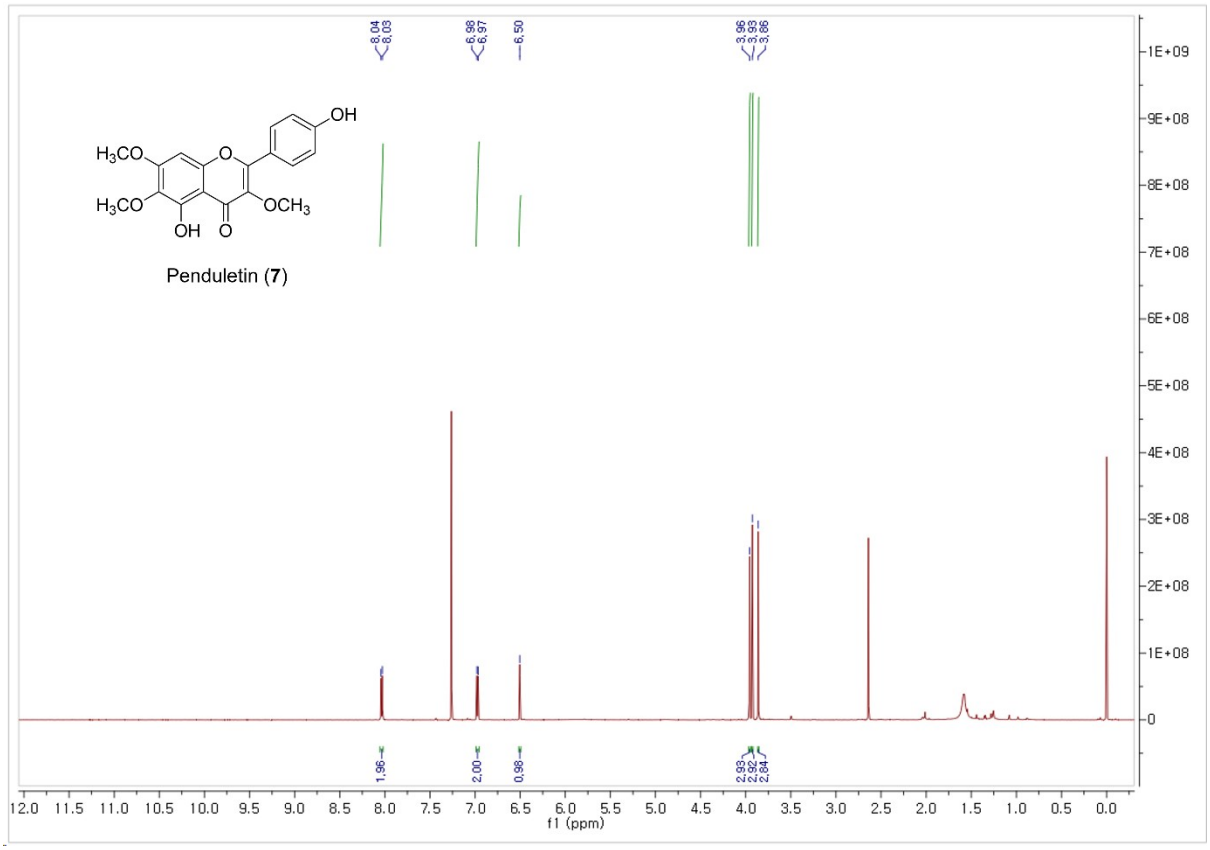


Figure S19. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound **7**

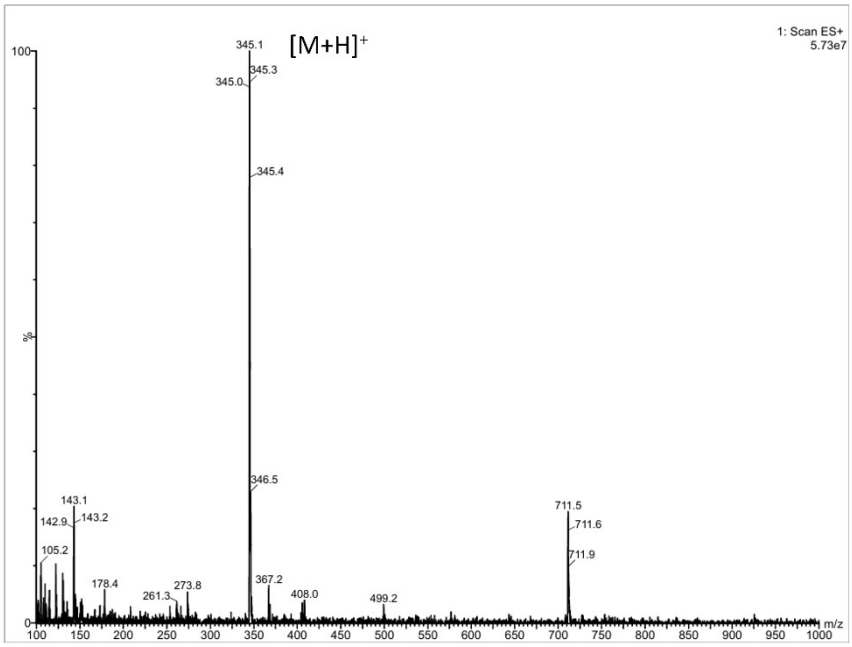


Figure S20. ESI-MS spectrum of compound **7**

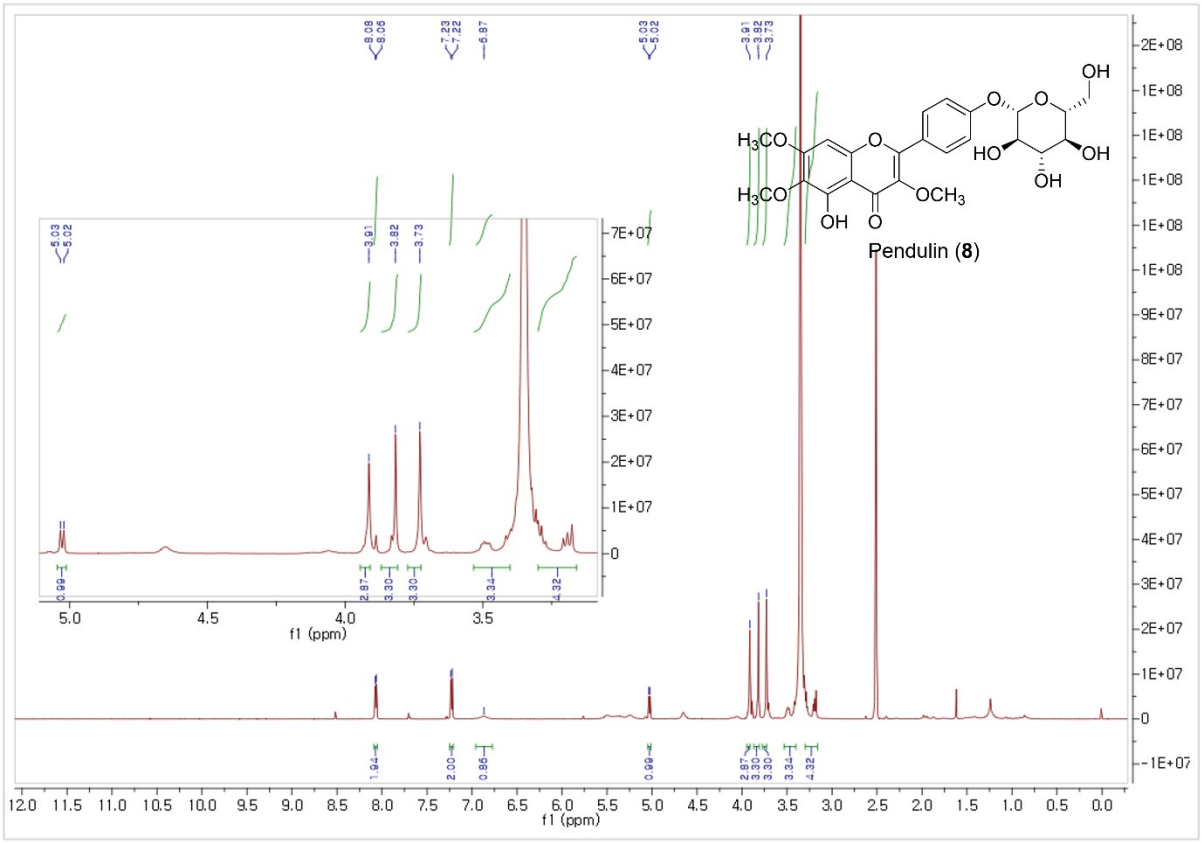


Figure S21. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of compound **8**

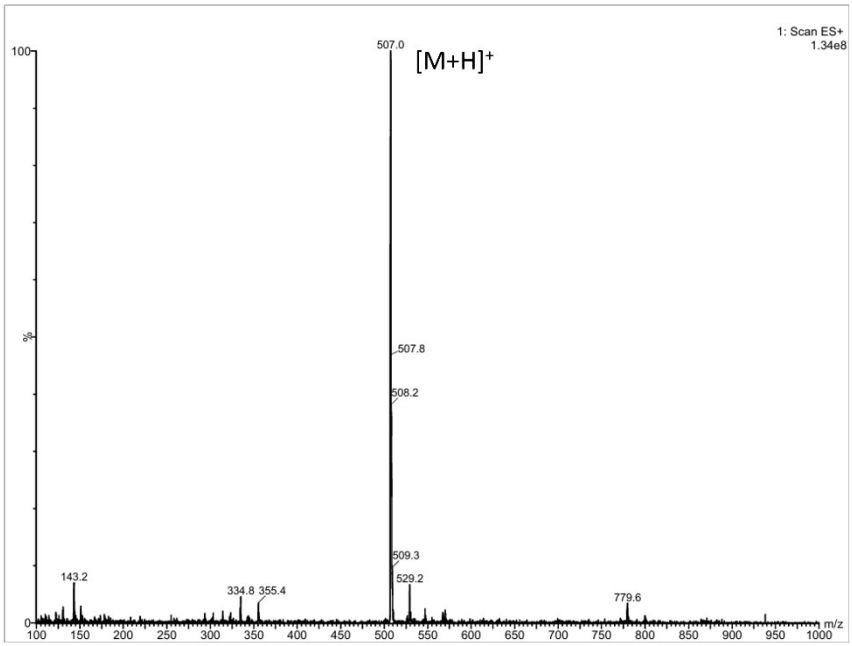


Figure S22. ESI-MS spectrum of compound **8**

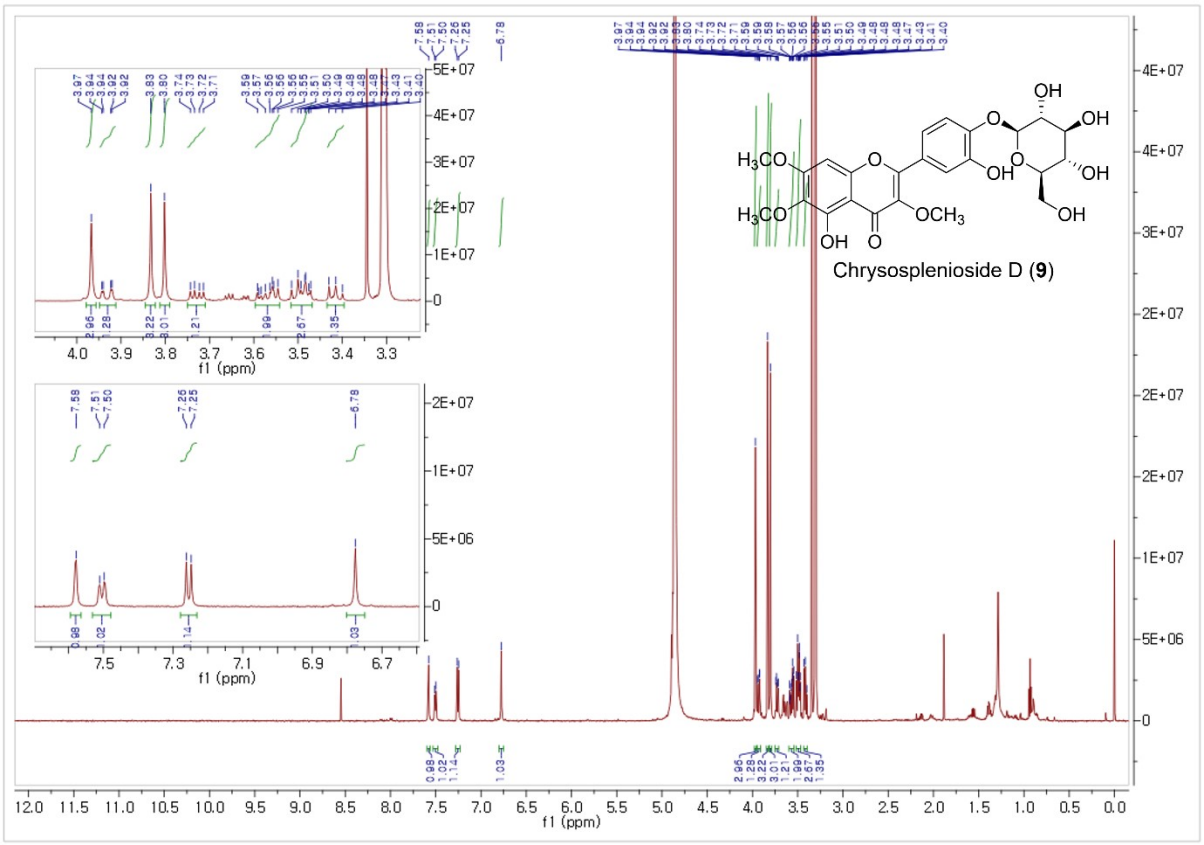


Figure S23. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **9**

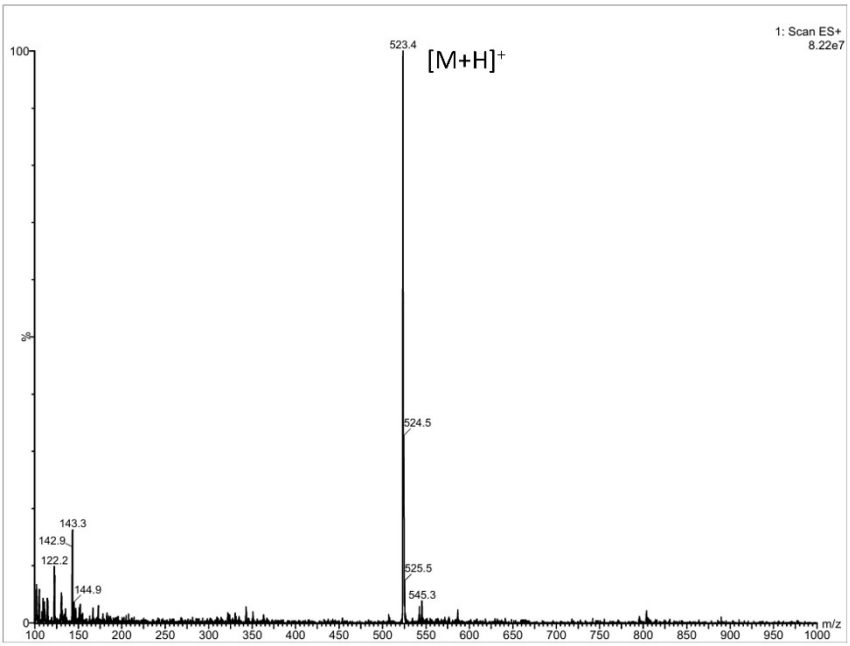


Figure S24. ESI-MS spectrum of compound **9**

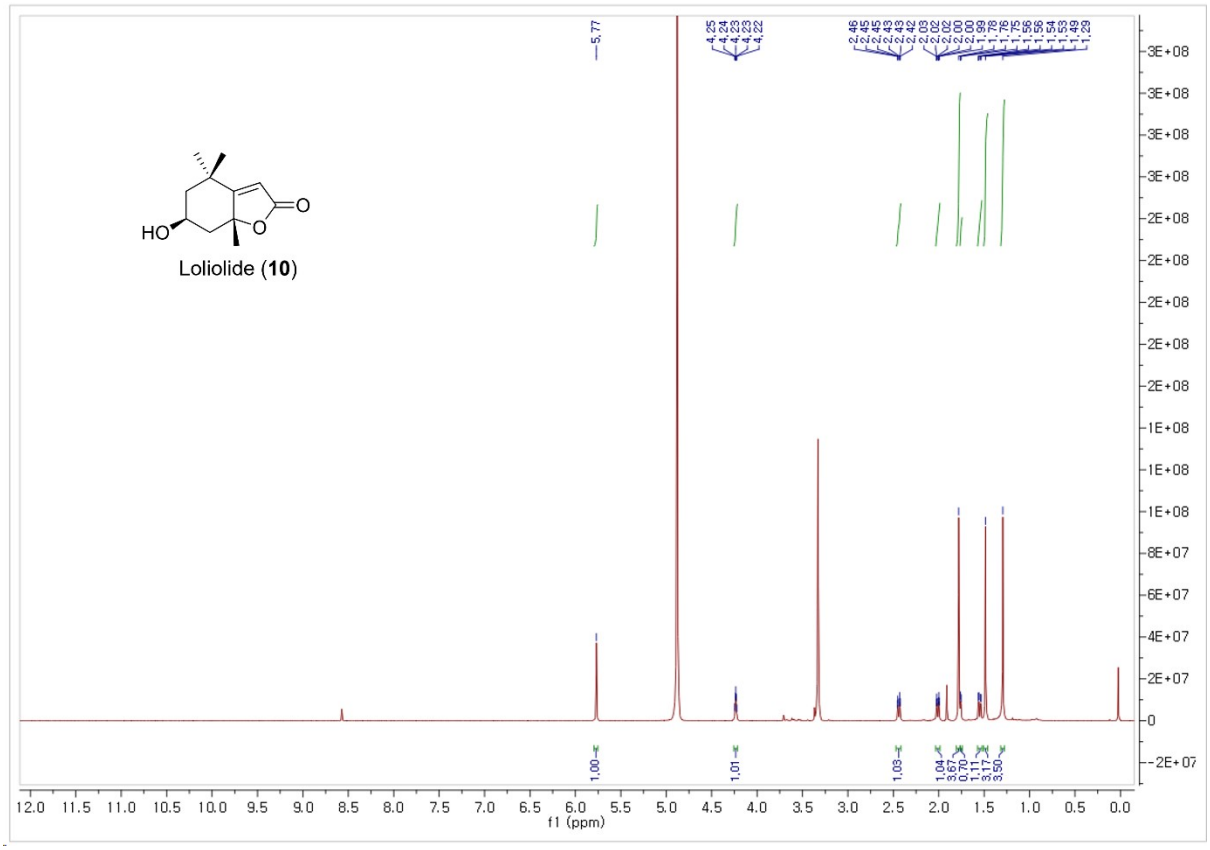


Figure S25. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **10**

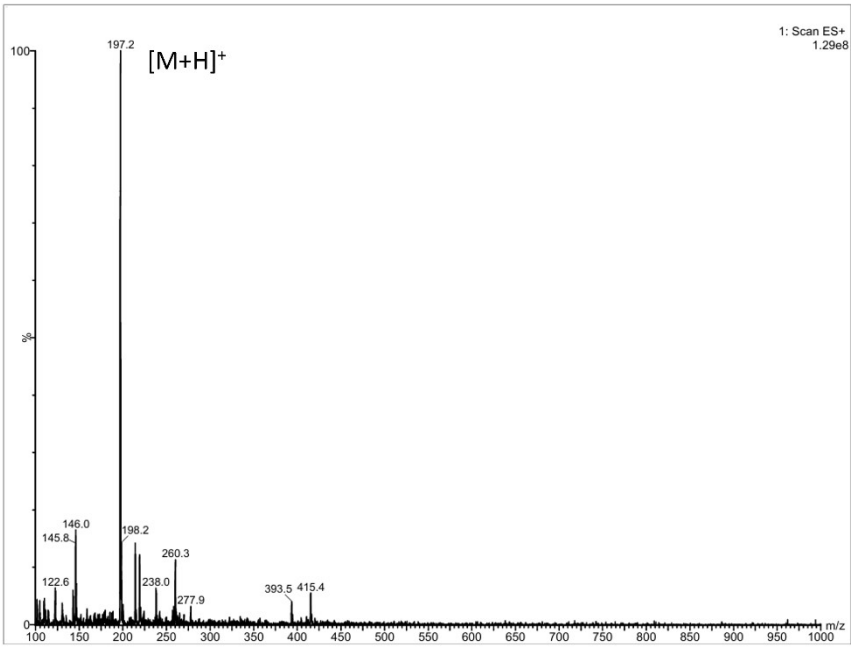


Figure S26. ESI-MS spectrum of compound **10**

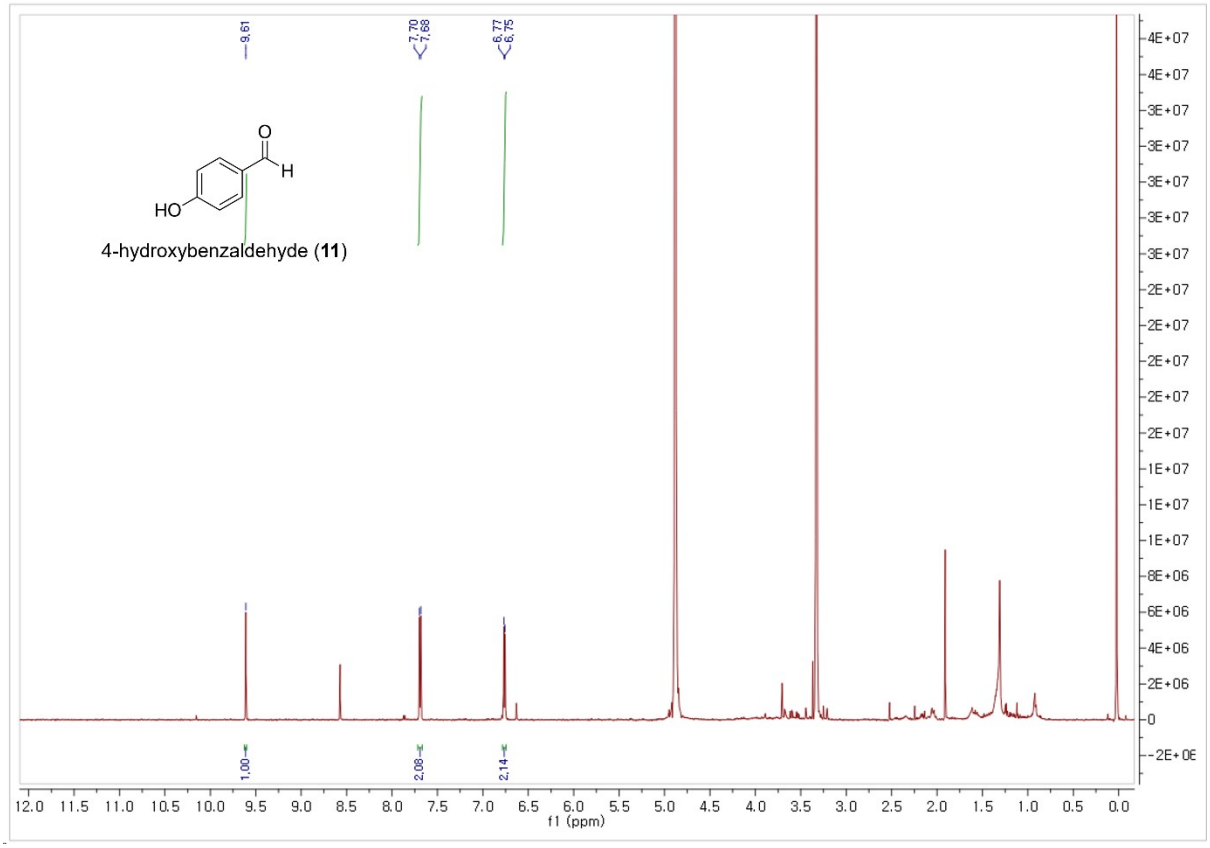


Figure S27. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **11**

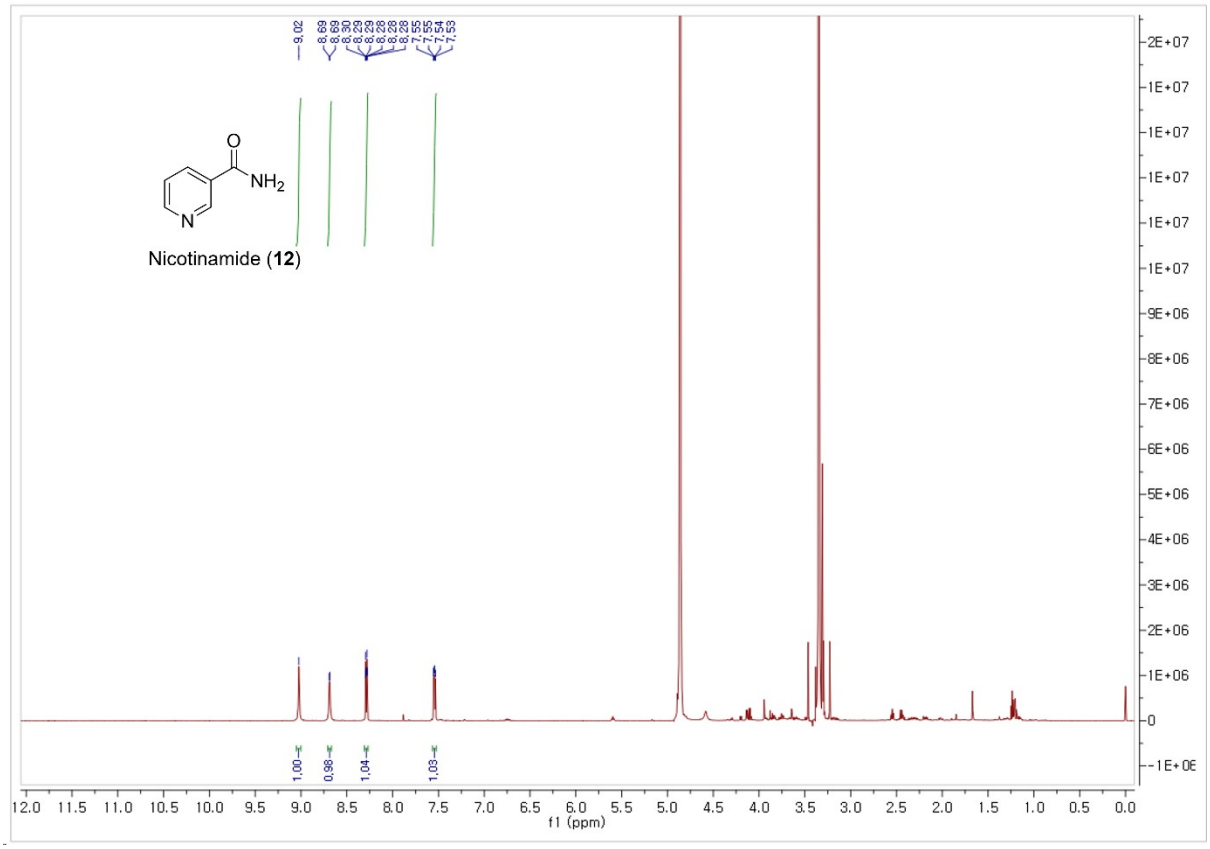


Figure S28. ^{1}H NMR spectrum (600 MHz, CD_3OD) of compound **12**

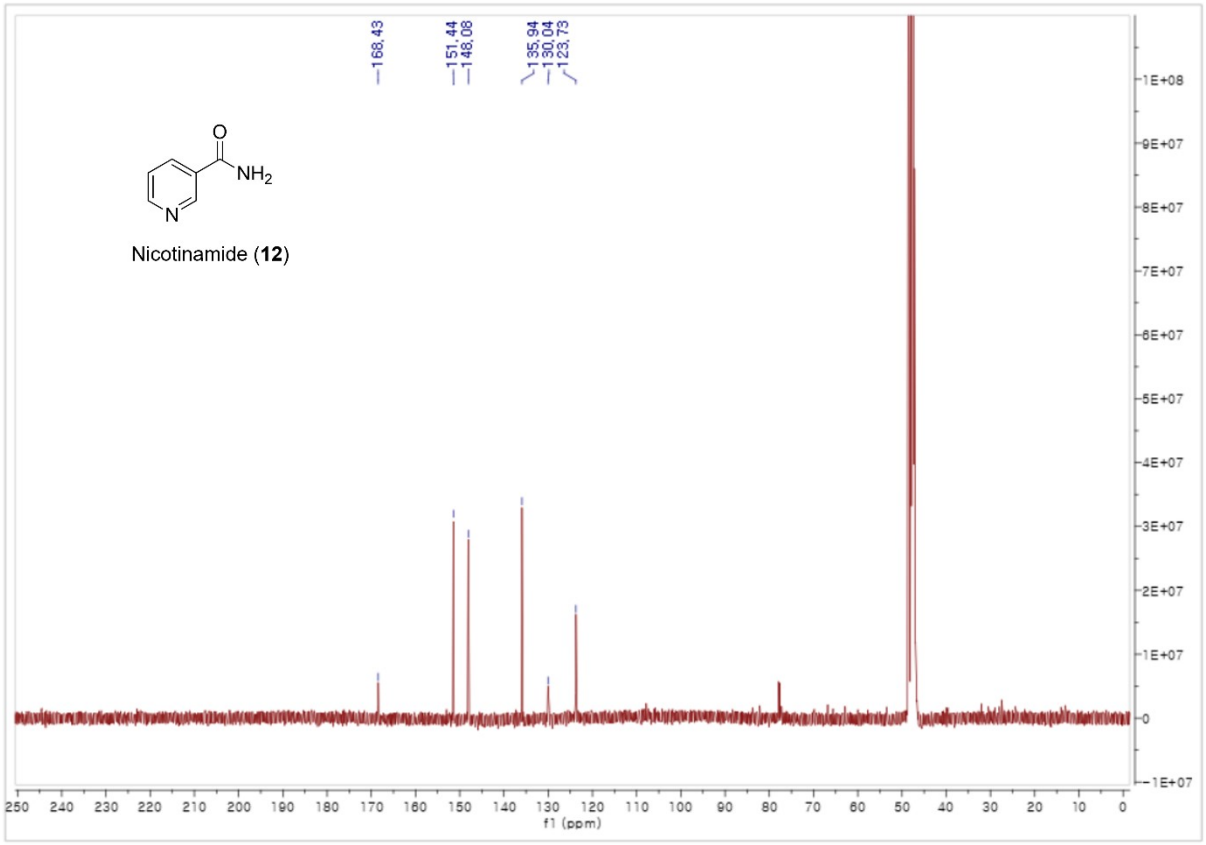
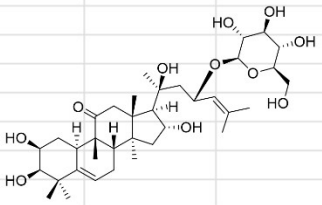


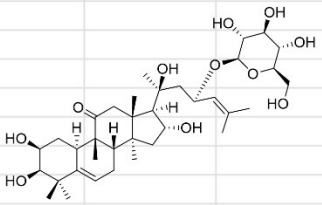
Figure S29. ^{13}C NMR spectrum (150 MHz, CD_3OD) of compound **12**

Functional	Solvent?	Basis Set	Type of Data
B3LYP	Gas Phase	6-31G(d,p)	Unscaled Shifts

		DP4+	100.00%	0.00%	-	-	-
Nuclei	sp2?	Experimental	Isomer 1	Isomer 2	Isomer 3	Isomer 4	Isomer 5
c	0	28.43	30.6197668	30.6008977			
c	0	67.86	67.1640533	67.5488146			
c	0	78.59	78.2383026	77.4086168			
c	0	41.35	44.0735367	43.9118747			
c	x	138.33	136.107348	136.763788			
c	x	119.8	118.986371	118.167982			
c	0	23.47	25.8223151	25.9785042			
c	0	43.19	44.961196	44.7197257			
c	0	48.54	50.7628367	50.7807795			
c	0	33.69	36.6442134	36.4571262			
c	x	215.53	205.420489	205.555929			
c	0	48.58	48.1965455	48.1366351			
c	0	50.66	53.8945971	53.698379			
c	0	48.16	51.1422753	51.4904021			
c	0	45.02	43.9365419	45.930173			
c	0	71.82	72.7292462	73.0106112			
c	0	58.38	59.2041176	61.9171225			
c	0	19.06	20.3324992	19.3228447			
c	0	18.92	21.9766358	21.7068668			
c	0	74.11	72.8574196	76.2275976			
c	0	26.03	28.2675799	24.2474902			
c	0	48.58	54.5728147	44.8607557			
c	0	70.11	69.6804376	78.6622465			
c	x	125.11	121.866605	121.997084			
c	x	135.9	134.14719	134.340696			
c	0	24.48	24.9900651	24.9554584			
c	0	17.04	17.1773917	16.9725495			
c	0	26.18	25.0096351	25.0688808			
c	0	24.75	25.9282277	26.1538998			
c	0	18.31	17.5796474	17.0810736			
c	0	98.86	98.7588772	106.356909			



Isomer 1 (23*S*)
DP4+: 100%



Isomer 1 (23*R*)
DP4+: 0%

Figure S30. Results of DP4+ analysis of **1** (Isomer 1, 23*S*-**1**; Isomer 2, 23*R*-**1**)

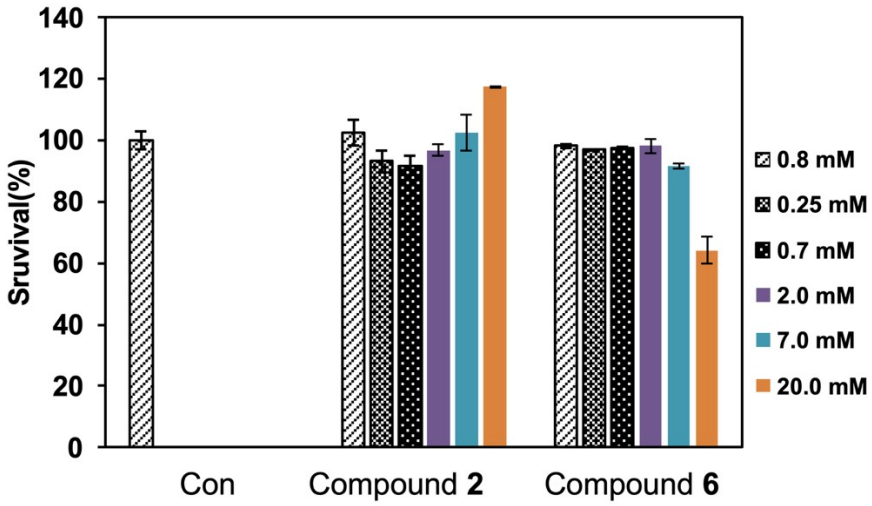


Figure S31. *In vitro* cell viability results of compounds **2** and **6**

Table S1. Gibbs free energies and Boltzmann distribution of conformers (23*S*-**1**)

Conformers	B3LYP/6-31G(d,p) Gibbs free energy (298.15 K)		
	G (Hartree)	ΔG (kcal/mol)	Boltzmann distribution
23*S*-**1**_6	-2232.838503	0.00	21.79225%
23*S*-**1**_7	-2232.838494	0.01	21.57595%
23*S*-**1**_3	-2232.838407	0.06	19.67360%
23*S*-**1**_4	-2232.838396	0.07	19.46301%
23*S*-**1**_12	-2232.836998	0.94	4.42371%
23*S*-**1**_15	-2232.836996	0.95	4.41519%
23*S*-**1**_1	-2232.836464	1.28	2.51380%
23*S*-**1**_2	-2232.836426	1.30	2.41447%
23*S*-**1**_14	-2232.83569	1.77	1.10745%
23*S*-**1**_11	-2232.835314	2.00	0.74409%
23*S*-**1**_10	-2232.834791	2.33	0.42751%
23*S*-**1**_9	-2232.834745	2.36	0.40709%
23*S*-**1**_5	-2232.834659	2.41	0.37175%
23*S*-**1**_8	-2232.834612	2.44	0.35360%
23*S*-**1**_13	-2232.834507	2.51	0.31654%

Table S2. Gibbs free energies and Boltzmann distribution of conformers (23*R*-**1**)

Conformers	B3LYP/6-31G(d,p) Gibbs free energy (298.15 K)		
	G (Hartree)	ΔG (kcal/mol)	Boltzmann distribution
23*R*-**1**_7	-2232.840311	0.00	57.01771%
23*R*-**1**_12	-2232.839909	0.25	37.24763%
23*R*-**1**_20	-2232.838032	1.43	5.10366%
23*R*-**1**_26	-2232.835161	3.23	0.24391%
23*R*-**1**_2	-2232.834294	3.78	0.09740%
23*R*-**1**_6	-2232.833832	4.07	0.05971%
23*R*-**1**_4	-2232.833754	4.11	0.05496%
23*R*-**1**_8	-2232.833588	4.22	0.04609%
23*R*-**1**_23	-2232.833245	4.43	0.03206%
23*R*-**1**_17	-2232.832463	4.92	0.01401%
23*R*-**1**_10	-2232.832396	4.97	0.01304%
23*R*-**1**_13	-2232.832392	4.97	0.01299%
23*R*-**1**_21	-2232.832145	5.12	0.01000%
23*R*-**1**_1	-2232.832134	5.13	0.00989%
23*R*-**1**_19	-2232.832131	5.13	0.00985%
23*R*-**1**_9	-2232.831965	5.24	0.00827%
23*R*-**1**_5	-2232.831694	5.41	0.00621%
23*R*-**1**_15	-2232.831598	5.47	0.00560%
23*R*-**1**_3	-2232.831242	5.69	0.00384%
23*R*-**1**_18	-2232.83106	5.80	0.00317%

Table S3. Experimental (Exp.) and calculated (Cal.) ^{1}H and ^{13}C chemical shift values and its possible isomer 23*S*-**1** and 23*R*-**1** used for DP4+ analysis

Carbon	Exp.	Cal.		Proton	Exp.	Cal.	
	1	23*S*-**1**	23*R*-**1**		**1**	23*S*-**1**	23*R*-**1**
1	28.43	30.61977	30.6009	1α	1.42	2.186212	2.127682
2	67.86	67.16405	67.54881	1β	1.36	1.777567	1.824961
3	78.59	78.2383	77.40862	2	3.8	4.262658	4.320204
4	41.35	44.07354	43.91187	3	3.26	3.943628	3.978491
5	138.33	136.1073	136.7638	6	5.58	6.466632	6.383258
6	119.80	118.9864	118.168	7α	2.32	2.89248	2.875881
7	23.47	25.82232	25.9785	7β	1.86	2.487997	2.357224
8	43.19	44.9612	44.71973	8	1.83	2.367222	2.303331
9	48.54	50.76284	50.78078	10	2.39	2.858824	2.897986
10	33.69	36.64421	36.45713	12α	2.37	2.864625	3.068867
11	215.53	205.4205	205.5559	12β	3.18	3.480716	3.568654
12	48.58	48.19655	48.13664	15α	1.76	2.463545	2.333477
13	50.66	53.8946	53.69838	15β	1.38	2.140099	1.63664
14	48.16	51.14228	51.4904	16	4.48	5.4367	5.438833
15	45.02	43.93654	45.93017	17	2.48	2.779306	2.494401
16	71.82	72.72925	73.01061	18	0.77	1.509612	1.47902
17	58.38	59.20412	61.91712	19	1.01	1.61881	1.597004
18	19.06	20.3325	19.32284	21	1.33	1.61725	1.962712
19	18.92	21.97664	21.70687	22	1.5	1.72308	3.116236
20	74.11	72.85742	76.2276	22	2.07	2.672233	1.776684
21	26.03	28.26758	24.24749	23	4.84	5.537793	5.278745
22	48.58	54.57281	44.86076	24	5.04	5.689804	5.961264
23	70.11	69.68044	78.66225	26	1.65	2.201564	2.201564
24	125.11	121.8666	121.9971	27	1.63	2.264308	2.283987
25	135.90	134.1472	134.3407	28	0.95	1.704363	1.704363
26	24.48	24.99007	24.95546	29	1.09	1.521751	1.518481
27	17.04	17.17739	16.97255	30	1.22	1.890803	1.882292
28	26.18	25.00964	25.06888	1′	4.09	4.669886	4.851644
29	24.75	25.92823	26.1539	2′	3.08	3.559356	3.488059
30	18.31	17.57965	17.08107	3′	3.19	3.854897	3.910852
1′	98.86	98.75888	106.3569	4′	3.1	3.709907	3.756824
2′	73.56	73.15186	72.96672	5′	3.07	3.844415	3.83384
3′	76.78	76.0103	76.40899	6′	3.78	4.458449	4.398545
4′	70.62	69.94536	70.367	6’	3.53	3.997411	4.059218
5′	76.86	79.43351	76.9393				
6′	61.66	60.95559	61.83522				

Table S4. Linear regression data for the quantitation analysis of compound **6**

Parameter	**Compound 6 (Cirsimaritin)**
Concentration Range (mg/mL)	0.5─0.015625
Regression equation	$y = 6788x + 21{,}664$
Correlation coefficient (R^2)	0.9992
Slope	6788
Average content (mg/g)	17.37