Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supplementary Information

Lithocarpins A-D, Four Tenellone−Macrolide Conjugated [4+2] Hetero-adducts from the Deep-sea Derived Fungus *Phomopsis lithocarpus* FS508

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X-ray crystallographic data

X-ray crystallographic data for lithocarpin A (1): $C_{38}H_{43}Cl_3O_{11}$, M = 782.07, monoclinic, size 0.15 × 0.13 × 0.11 mm^3, space group $P2_1$; a = 12.0999 (3) Å, b = 8.9388 (2) Å, c = 17.0397 (4) Å, α =β = 90.00°, γ =90.378°, V = 1842.95 (8) Å^3, T = 100.00 K, Z = 2, ρ_{calcd} = 1.409 g/cm^3, F(000) = 820.0, 17295 reflections in $-14 \le h \le 15$, $-10 \le k \le 11$, $-20 \le l \le 20$, measured in the range 7.31° ≤ θ ≤ 147.52°, GOOF = 1.036, Final R indices [I > 2σ(I): R_1 = 0.0906, wR_2 = 0.2611, Final R indices (all data): R_1 = 0.0940, wR_2 = 0.2650, Flack parameter –0.087 (13), largest difference peak and hole = 1.20 and –1.44 e. Å^{-3}. Data were collected on Agilent Xcalibur Nova single-crystal diffractometer using CuKα radiation. The crystal structure was refined by full-matrix least-squares calculation. Crystallographic data for the structure of lithocarpin A (**1**) reported in this paper have been deposited in the Cambridge Crystallographic Data Centre. (Deposition number: CCDC 1586451). Copies of these data can be obtained free of charge via www.ccdc.cam.au.ck/conts/retrieving.html.)

X-ray crystallographic data for lithocarpin D (4): $C_{37}H_{42}O_{11}$, M = 662.70, orthorhombic, size 0.14 × 0.13 × 0.11 mm^3, space group $P2_12_12_1$; a = 9.34542 (7) Å, b = 14.58845 (13) Å, c = 24.65138 (16) Å, α =β =γ = 90.00°, V = 3360.85 (4) Å^3, T = 100.01 K, Z = 4, ρ_{calcd} = 1.310 g/cm^3, F(000) = 1408.0, 38401 reflections in $-11 \le h \le 11$, $-17 \le k \le 15$, $-30 \le l \le 30$, measured in the range 7.04° ≤ θ ≤ 147.20°, GOOF = 1.047, Final R indices [I > 2σ(I): R_1 = 0.0340, wR_2 = 0.0889, Final R indices (all data): R_1 = 0.0349, wR_2 = 0.0897, Flack parameter –0.08 (5), largest difference peak and hole = 0.21 and –0.23 e. Å^{-3}. Data were collected on Agilent Xcalibur Nova single-crystal diffractometer using CuKα radiation. The crystal structure was refined by full-matrix least-squares calculation. Crystallographic data for the structure of lithocarpin D (**4**) reported in this paper have been deposited in the Cambridge Crystallographic Data Centre. (Deposition number: CCDC 1586450). Copies of these data can be obtained free of charge via www.ccdc.cam.au.ck/conts/retrieving.html.)

^{1}H and ^{13}C NMR data of compounds 1-4

Table S1 ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR data of **1** and **2** (δppm) in CD_3OD.

No.	**1**		**2**	
	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C
1		144.5, C		144.5, C
2		131.7, C		131.7, C
3		148.3, C		148.3, C
4	6.70, d, (8.3)	116.4, CH	6.69, d, (8.3)	116.4, CH
5	6.86, d, (8.3)	130.8, CH	6.85, m	130.9, CH
6		127.7, C		127.6, C
7	2.84, s	29.8, CH_2	2.85, t, (7.2)	29.8, CH_2
8	5.02, t, (6.5)	125.3, CH	5.03, d, (7.2)	125.2, CH
9		132.6, C		132.4, C
10	1.29, s	17.7, CH_3	1.30, s	17.7, CH_3
11	1.59, s	25.9, CH_3	1.59, s	25.7, CH_3
1'		125.1, C		125.1, C
2'		143.0, C		143.0, C
3'		145.0, C		145.0, C
4'	6.84, d, (2.0)	120.0, CH	6.85, d, (1.9)	120.0, CH
5'		131.4, C		131.2, C
6'	7.01, d, (2.0)	121.4, CH	7.06, d, (1.9)	121.5, CH
7'	2.36, s	21.0, CH_3	2.37, s	21.0, CH_3
8a'	4.39, dd, (10.2, 2.1)	65.6, CH_2	4.39, dd, (10.2, 2.1)	65.6, CH_2
8b'	3.79, t (10.2)		3.79, t (10.2)	
9'	3.67, dd, (10.2, 2.1)	79.6, CH	3.66, dd, (10.2, 2.1)	79.7, CH
10'		71.3, C		71.2, C
11'	0.67, s	23.6, CH_3	0.67, s	23.6, CH_3
12'	0.88, s	27.2, CH_3	0.86, s	27.2, CH_3
2"		168.5, C		168.1, C
3"	3.39, overlapped	56.0, CH	3.41, d, (5.0)	55.1, CH
4"	3.39, overlapped	52.4, CH	3.37, d, (5.0)	52.3, CH
5"	4.01, d, (4.5)	42.6, CH	4.11, d, (4.5)	43.0, CH
6"	3.31, d, (4.5)	57.1, CH	3.34, d, (4.5)	55.5, CH
7"		204.6, C		209.5, C
8"	5.63, dd, (4.0, 2.1)	76.1, CH	4.82, m	74.1, CH
9a"	2.08, m	38.8, CH_2	1.99, dd, (13.2, 2.4)	42.7, CH_2
9b"	2.67, ddd, (16.2, 10.0, 4.0)		2.59, ddd, (13.2, 10.0, 2.4)	
10"	4.78, m	70.6, CH	4.82, m	70.0, CH
11"	1.29, s	20.2, CH_3	1.23, d, (6.4)	20.2, CH_3
12"		91.8, C		91.8, C
13"	5.75, s	79.2, CH	5.47, s	79.3, CH
14"		171.7, C		
15"	2.08, s	20.4, CH_3		

Table S2 ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR data of **3** and **4** (δppm) in CD_3OD.

NO.	**3**		**4**	
	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C
1		144.9, C		144.4, C
2		131.6, C		131.3, C
3		148.8, C		148.8, C
4	6.60, d, (8.3)	115.9, CH	6.60, d, (8.3)	116.2, CH
5	6.82, d, (8.3)	130.4, CH	6.70, d, (8.3)	129.9, CH
6		127.7, C		126.9, C
7a	2.70, m	29.5, CH_2	2.43, m	29.7, CH_2
7b			2.72, dd, (16.3, 6.4)	
8	5.02, t, (6.3)	125.6, CH	4.99, tdd, (6.4, 2.9, 1.4)	124.4, CH
9		132.5, C		132.8, C
10	1.29, s	17.8, CH_3	1.31, s	20.3, CH_3
11	1.64, s	25.8, CH_3	1.63, s	25.8, CH_3
1'		125.1, C		125.5, C
2'		142.9, C		142.7, C
3'		145.3, C		144.8, C
4'	6.82, d, (2.0)	119.7, CH	6.84, d, (2.0)	120.0, CH
5'		130.5, C		130.1, C
6'	6.99, d, (2.0)	121.8, CH	7.49, d, (2.0)	121.9, CH
7'	2.35, s	21.0, CH_3	2.43, s	21.0, CH_3
8a'	4.35, m	65.7, CH_2	4.37, dd, (9.0, 1.8)	65.6, CH_2
8b'	3.85, m		3.78, t (9.0)	
9'	3.58, dd, (9.5, 2.1)	80.2, CH	3.61, m	79.9, CH
10'		71.3, C		71.2, C
11'	0.64, s	24.5, CH_3	0.66, s	23.8, CH_3
12'	0.77, s	26.2, CH_3	0.85, s	27.0, CH_3
2"		175.1, C		168.8, C
3a"	2.23, m	35.9, CH_2	3.61, overlapped	60.2, CH
3b"	2.35, m			
4a"	2.13, m	30.8, CH_2	3.61, overlapped	53.9, CH
4b"	2.23, m			
5"	3.38, m	46.8, CH	3.01, brs	45.5, CH
6"	3.07, d, (4.0)	56.8, CH	4.50, brs	56.5, CH
7"		215.9, C		204.6, C
8"	4.35, m	74.8, CH	5.54, brs	76.6, CH
9a"	2.03, m	44.2, CH_2	2.15, ddd, (12.4, 6.2, 3.0)	40.3, CH_2
9b"	2.23, m		2.56, t, (12.4)	
10"	5.30, m	67.7, CH	4.80, dqd, (9.4, 6.2, 3.0)	69.9, CH
11"	1.19, d, (5.3)	20.3, CH_3	1.33, s	17.7, CH_3
12"		92.4, C		93.1, C
13"	5.46, s	79.1, C	5.59, s	82.6, CH
14"				170.4, C
15"			1.88, s	20.8, CH_3

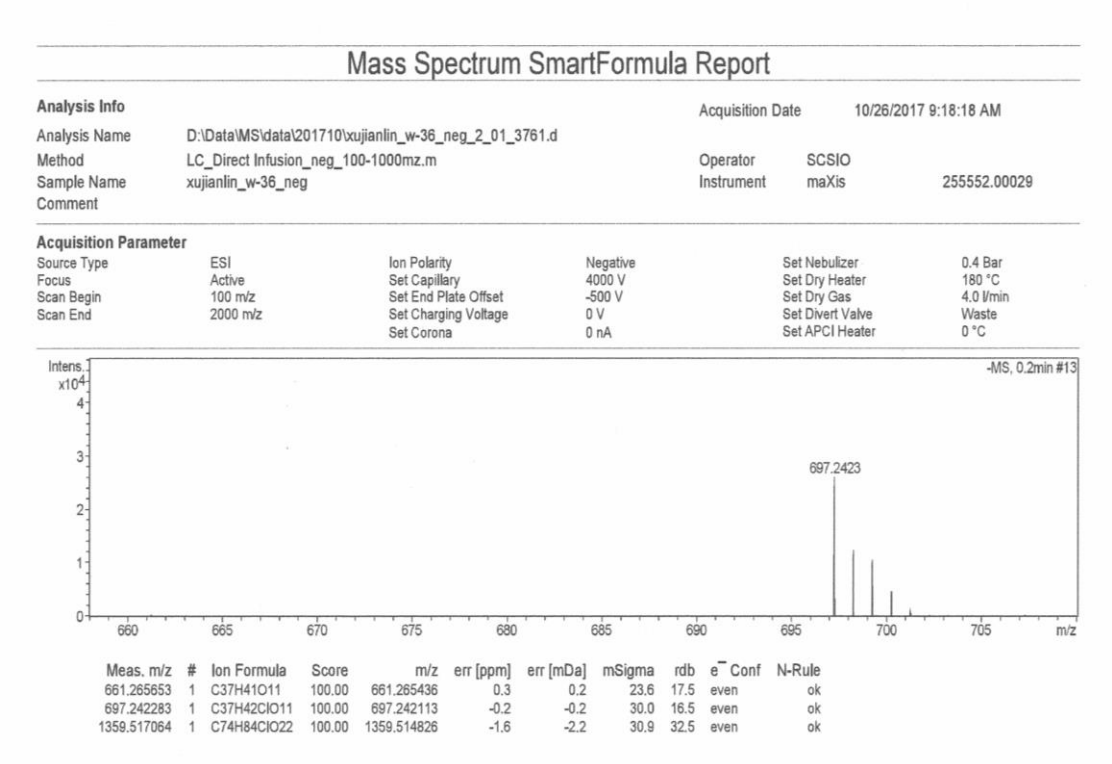

Figure S1. HRESIMS spectrum of lithocarpin A (**1**).

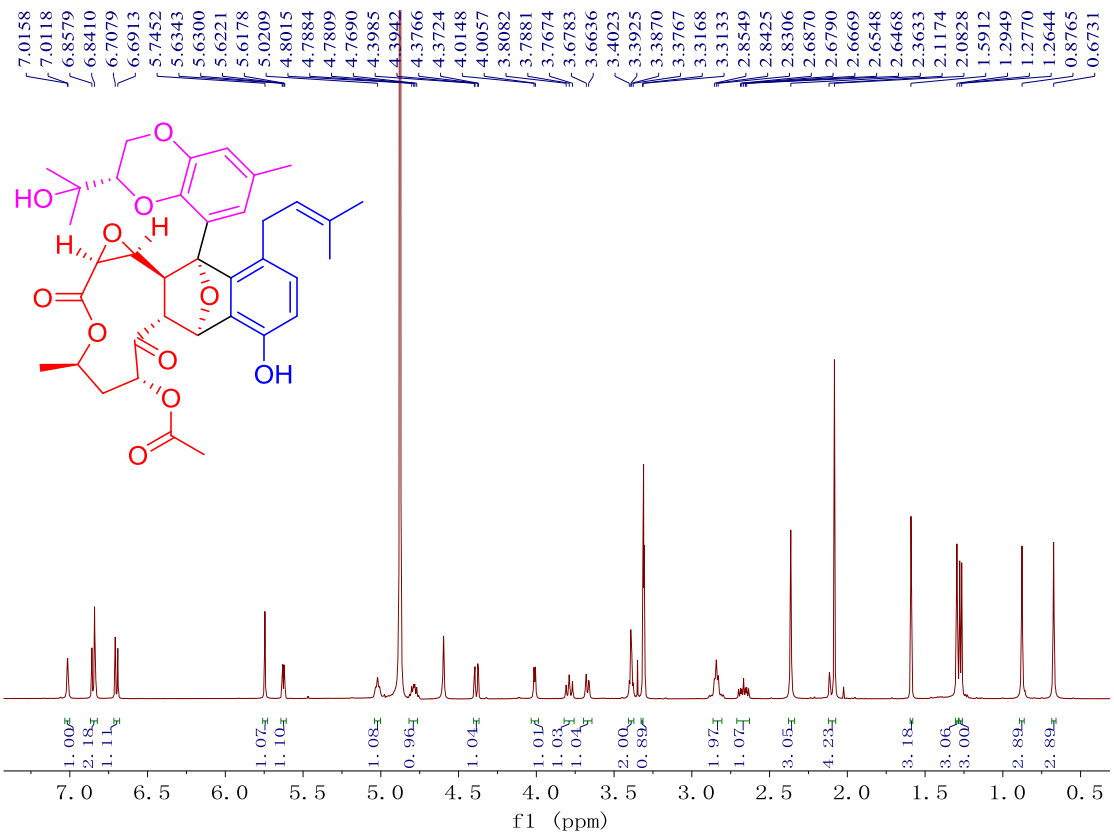

Figure S2. ^{1}H NMR spectrum (500 MHz, CD_3OD) of lithocarpin A (**1**).

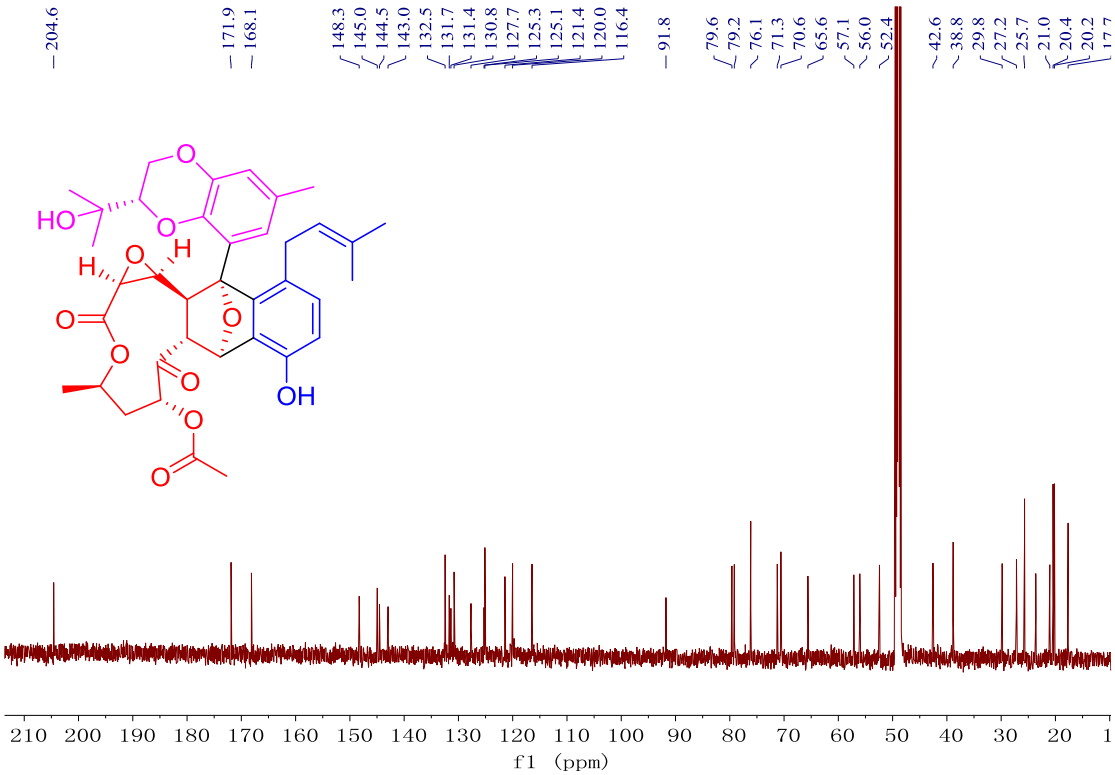

Figure S3. ^{13}C NMR spectrum (125 MHz, CD_3OD) of lithocarpin A (**1**).

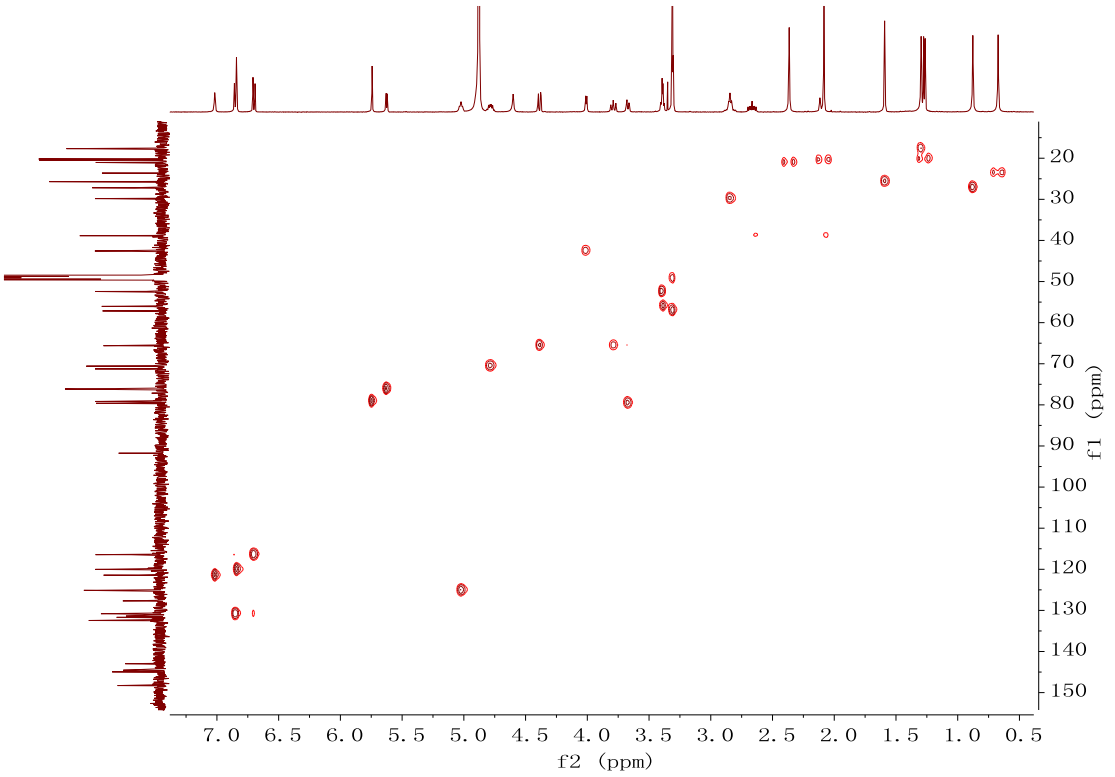

Figure S4. HSQC spectrum of lithocarpin A (**1**).

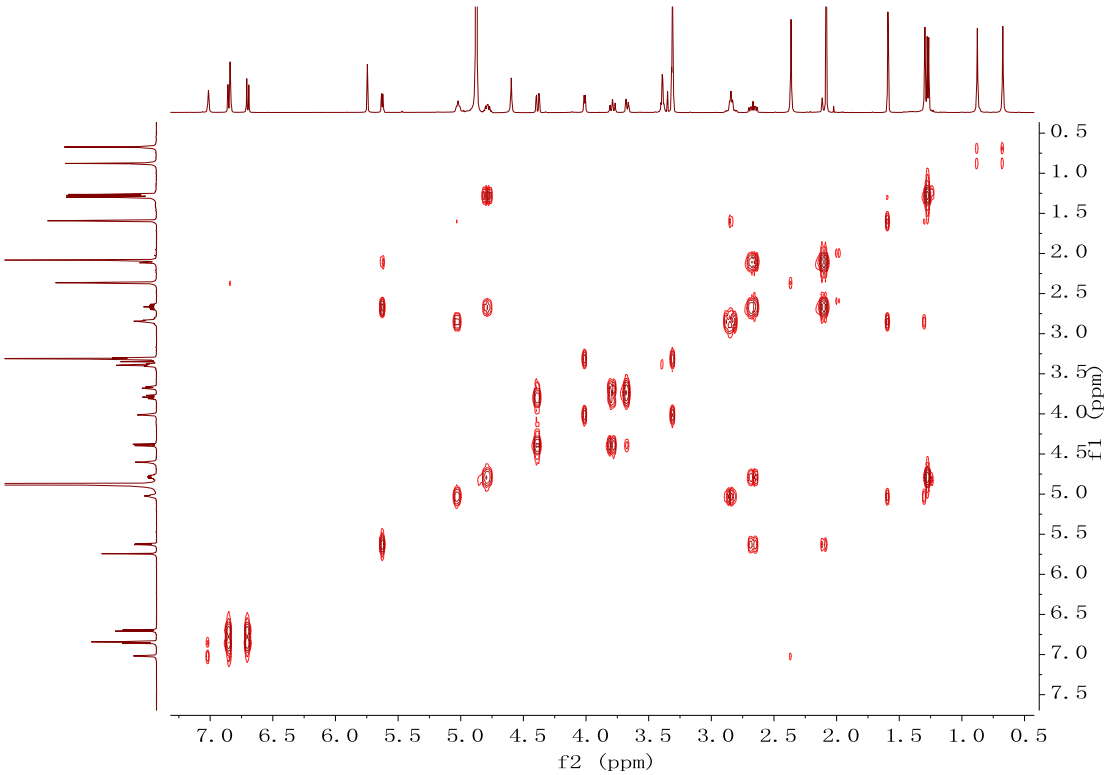

Figure S5. ^{1}H-^{1}H COSY spectrum (500 MHz, CD_3OD) of lithocarpin A (**1**).

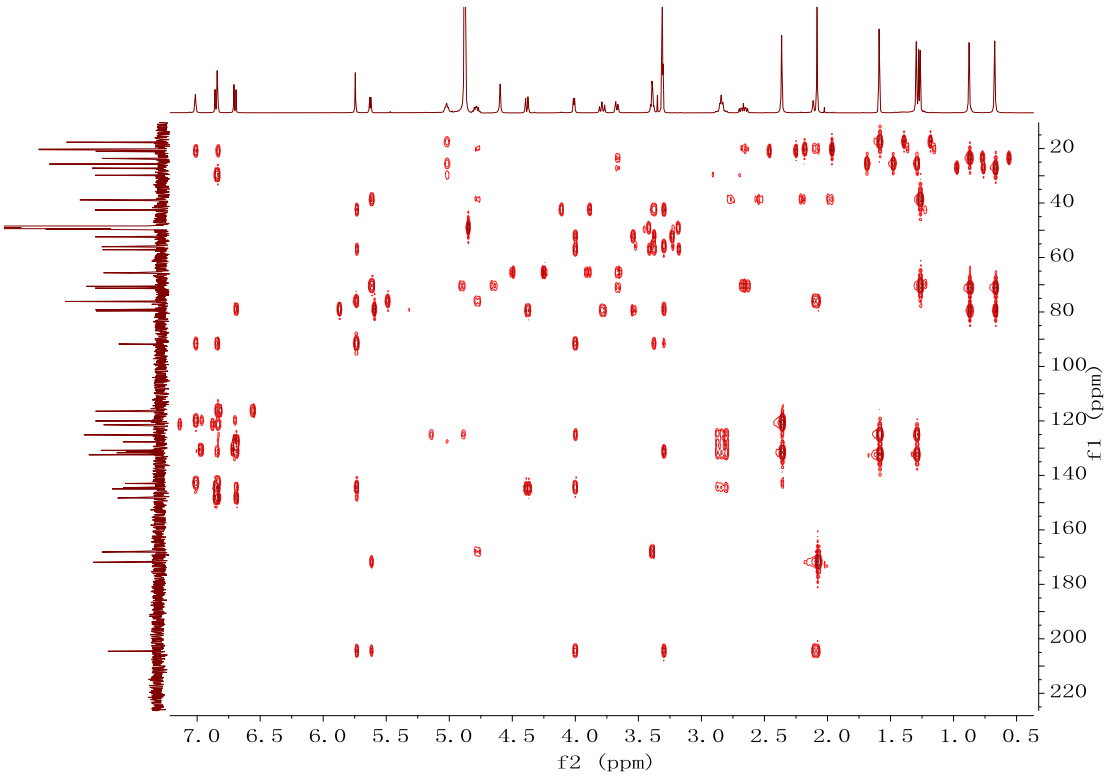

Figure S6. HMBC spectrum of lithocarpin A (**1**).

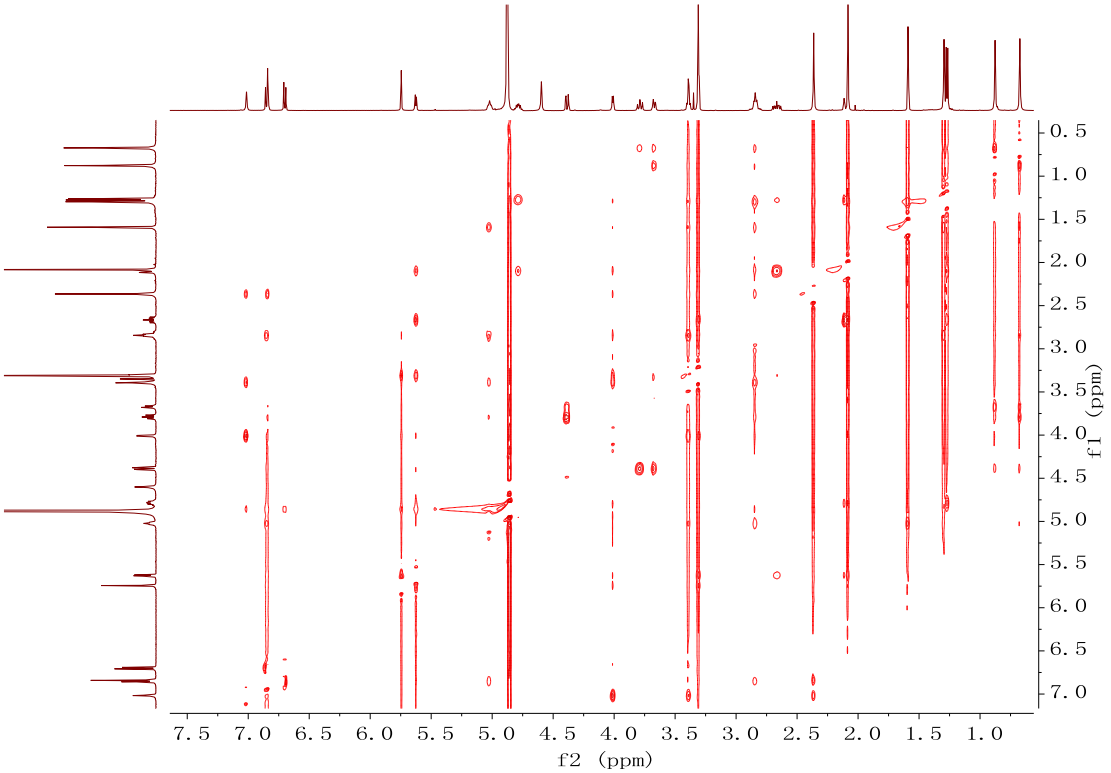

Figure S7. NOESY spectrum (500 MHz, CD_3OD) of lithocarpin A (**1**).

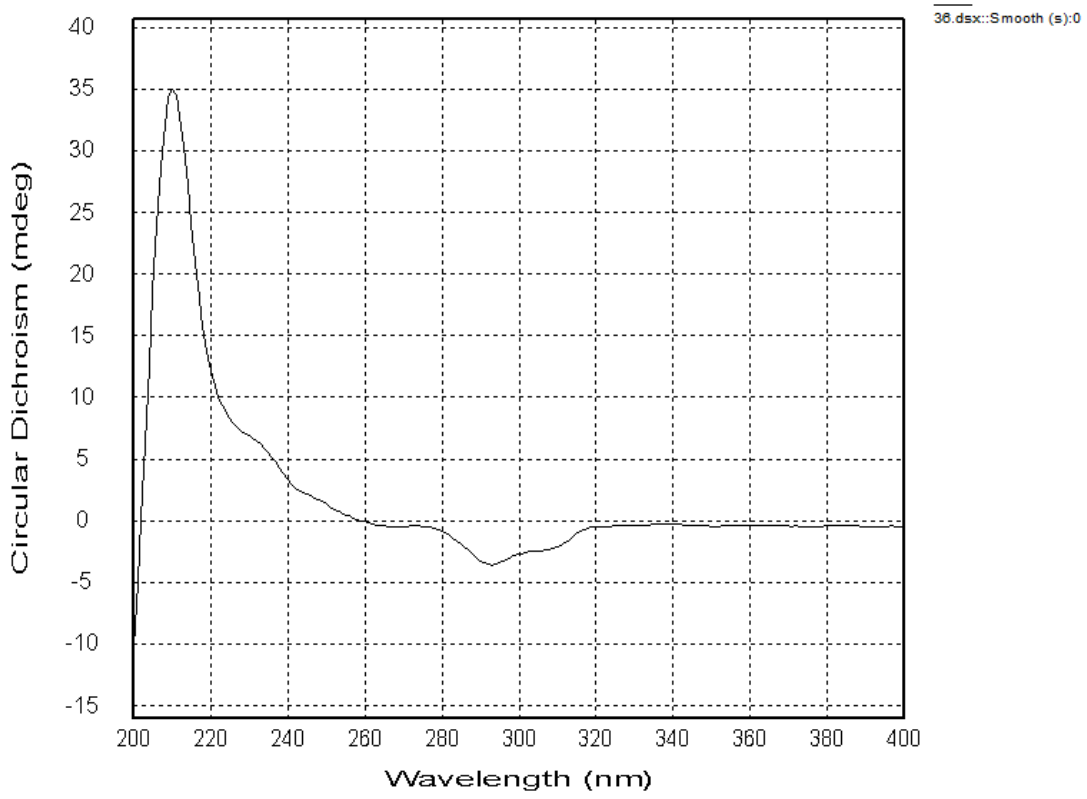

Figure S8. CD spectrum of lithocarpin A (**1**).

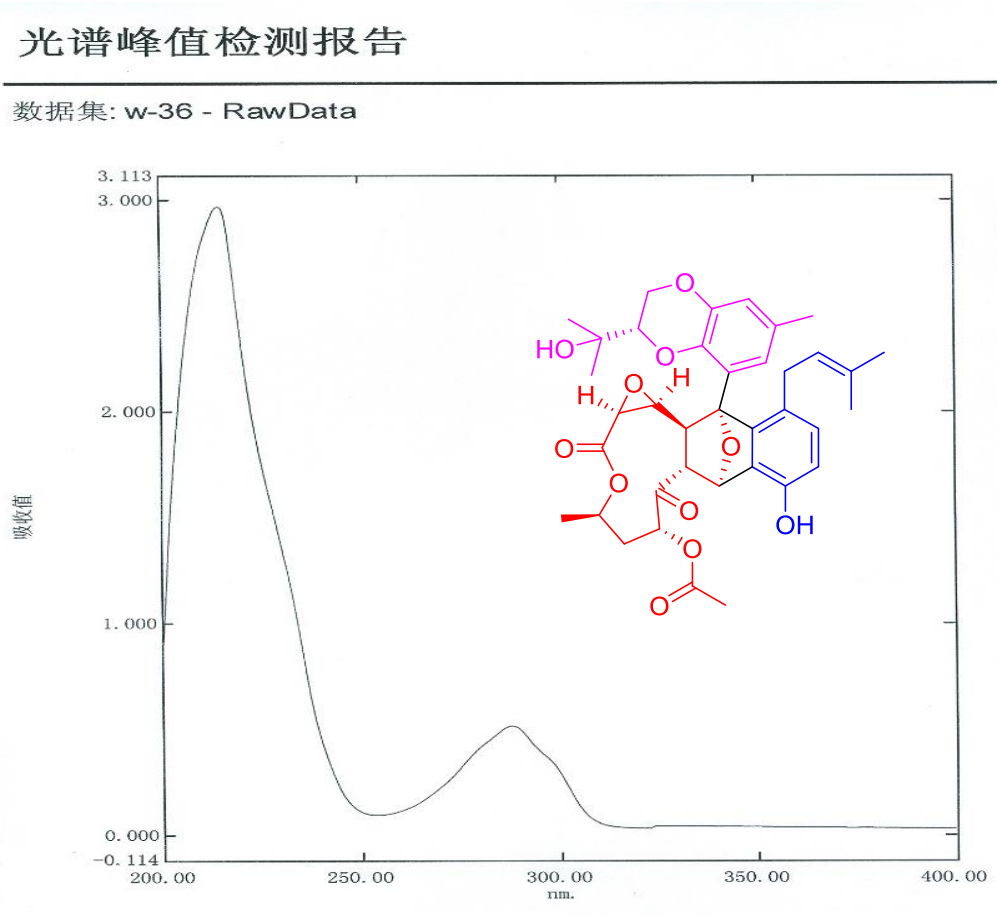

Figure S9. UV spectrum of lithocarpin A (**1**).

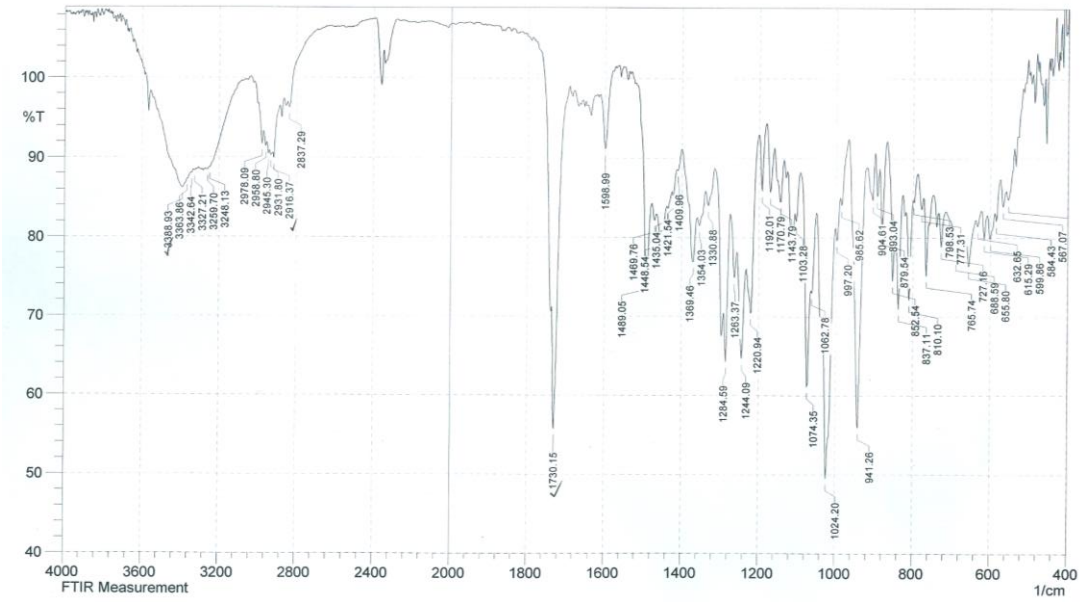

Figure S10. IR spectrum of lithocarpin A (**1**).

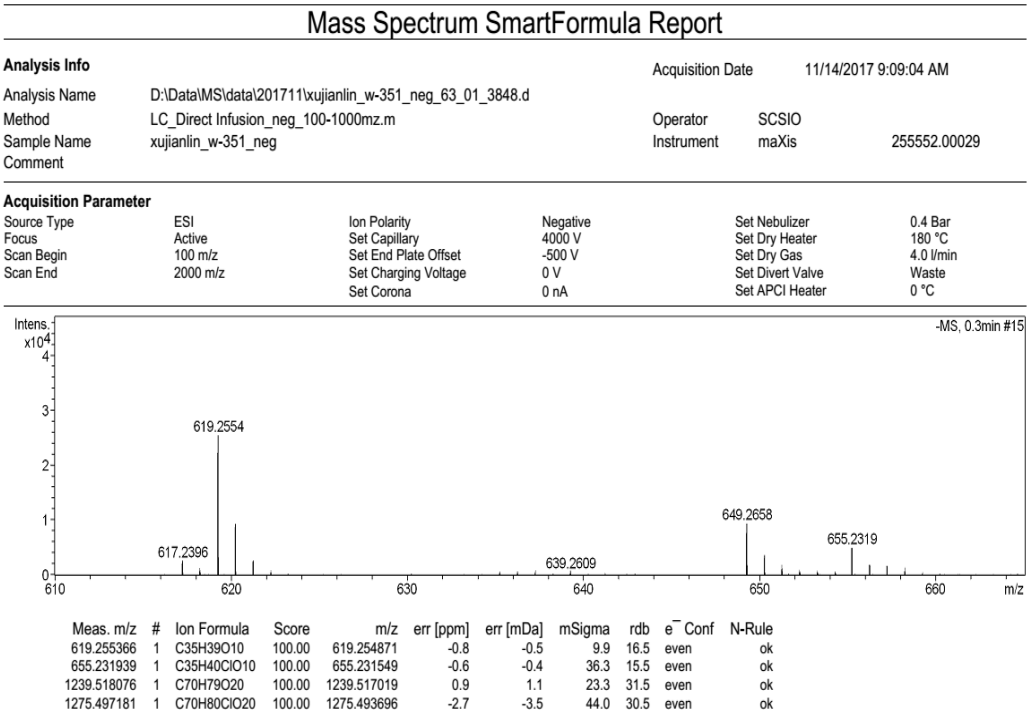

Figure S11. HRESIMS spectrum of lithocarpin B (**2**).

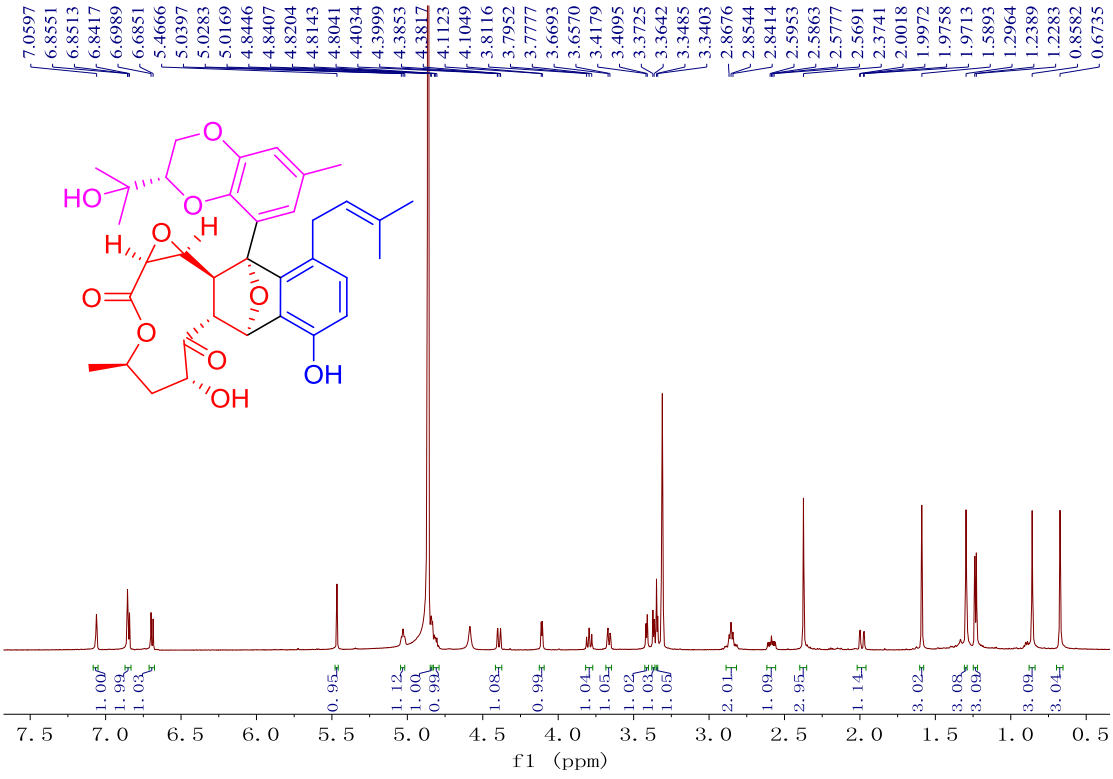

Figure S12. ^{1}H NMR spectrum (500 MHz, CD_3OD) of lithocarpin B (**2**).

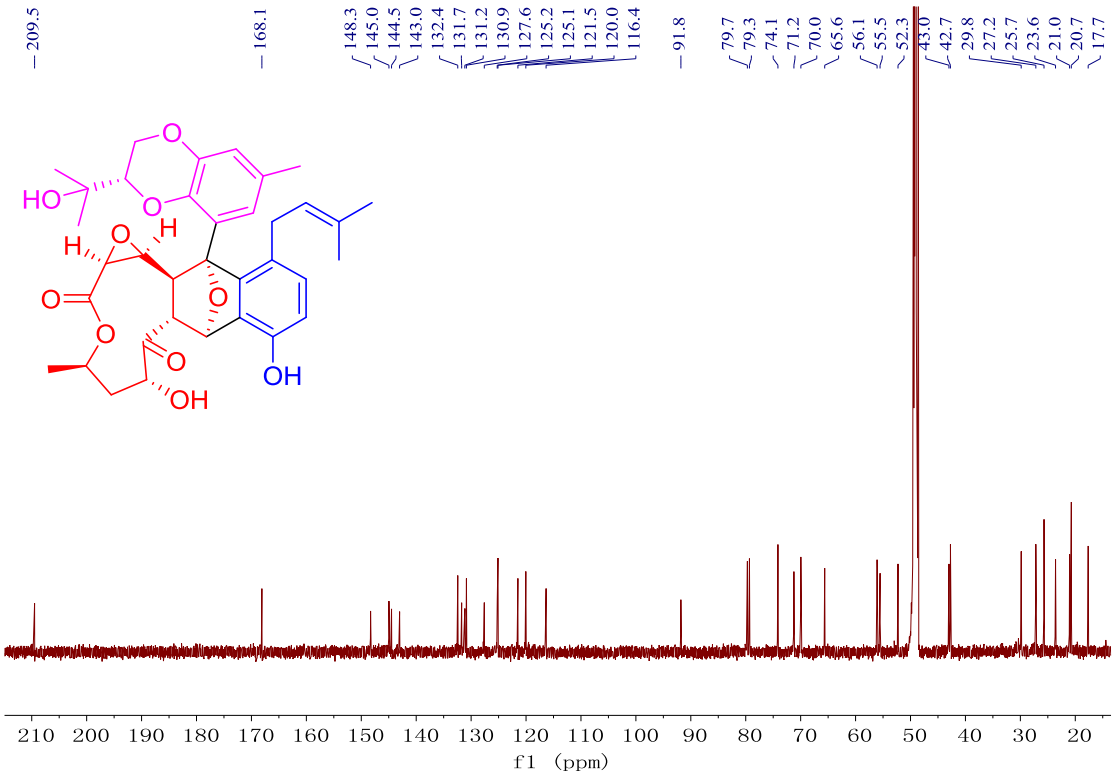

Figure S13. ^{13}C NMR spectrum (125 MHz, CD_3OD) of Lithocarpin B (**2**).

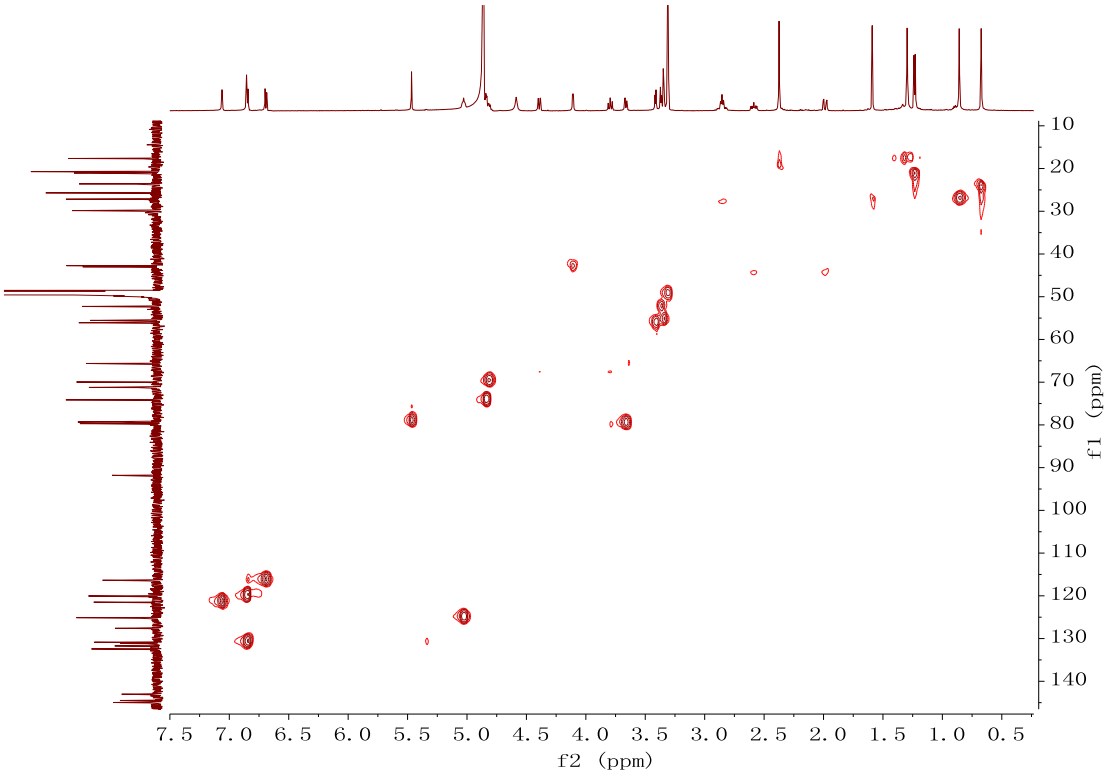

Figure S14. HSQC spectrum of lithocarpin B (**2**).

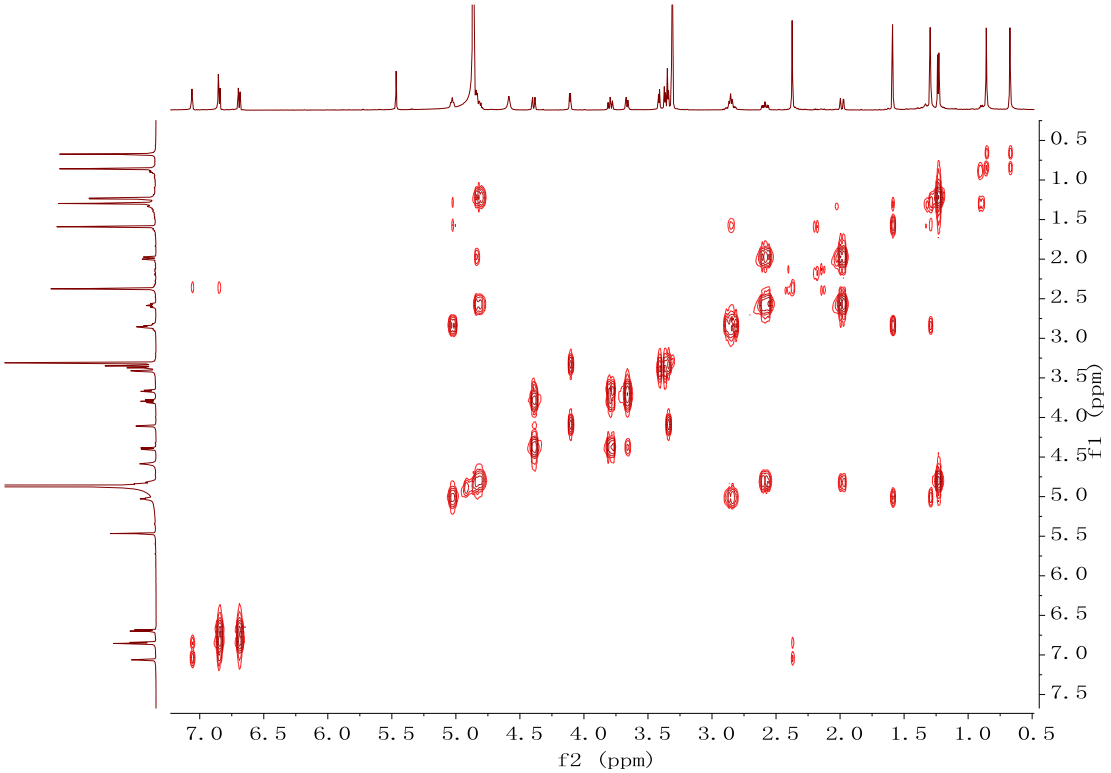

Figure S15. ^{1}H-^{1}H COSY spectrum (500 MHz, CD_3OD) of lithocarpin B (**2**).

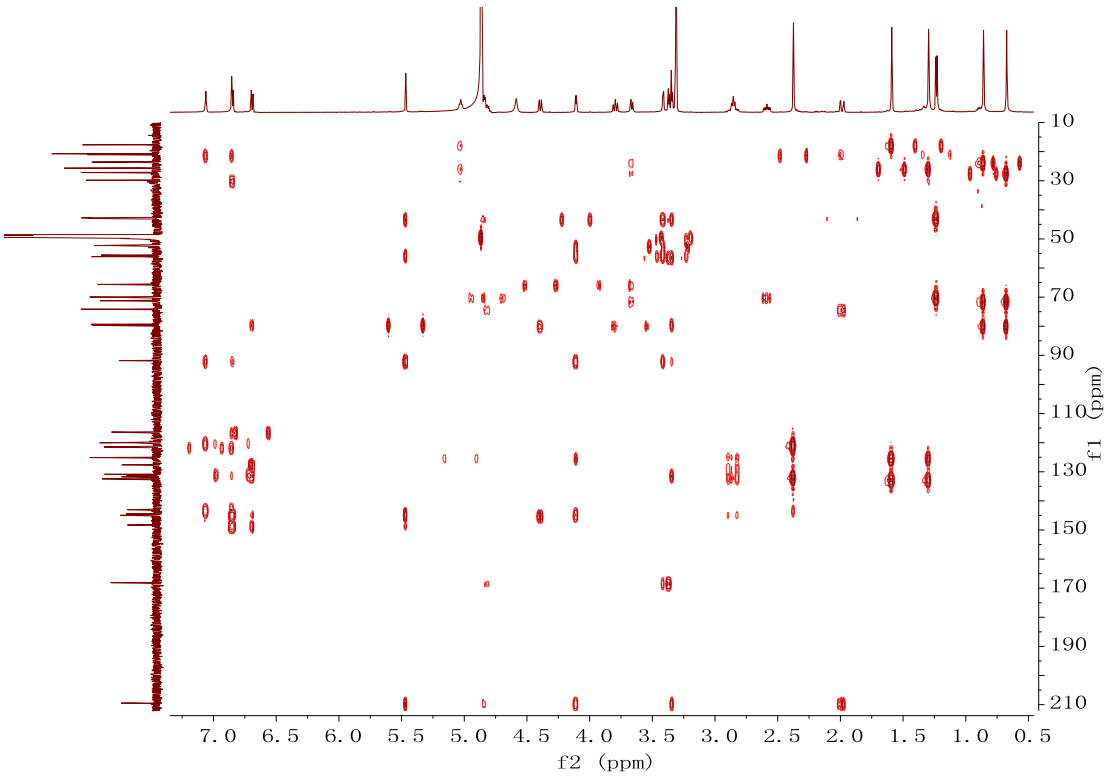

Figure S16. HMBC spectrum of lithocarpin B (**2**).

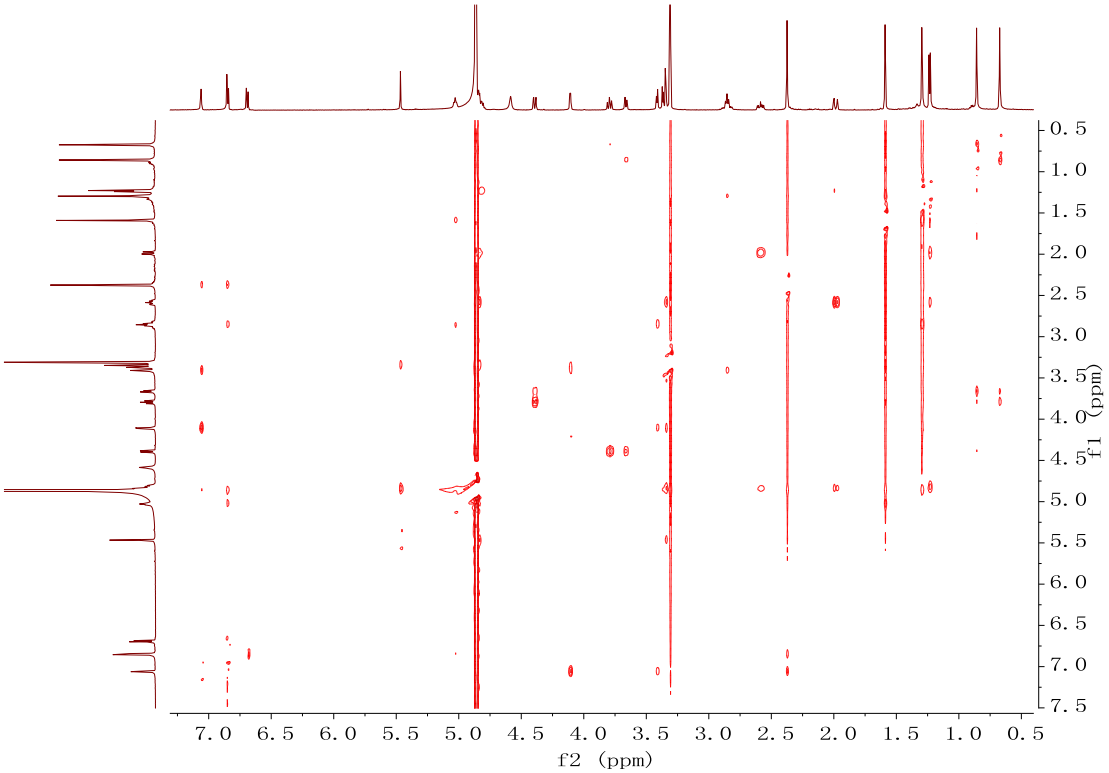

Figure S17. NOESY spectrum (500 MHz, CD_3OD) of lithocarpin B (**2**).

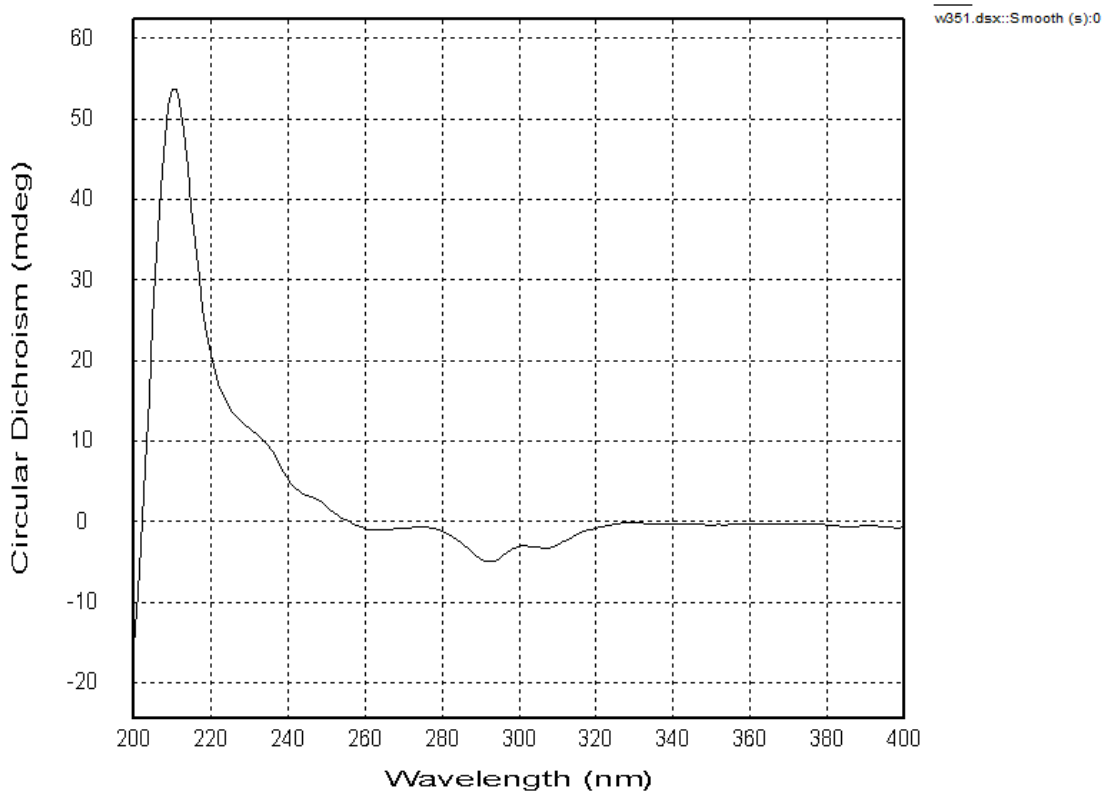

Figure S18. CD spectrum of lithocarpin B (**2**).

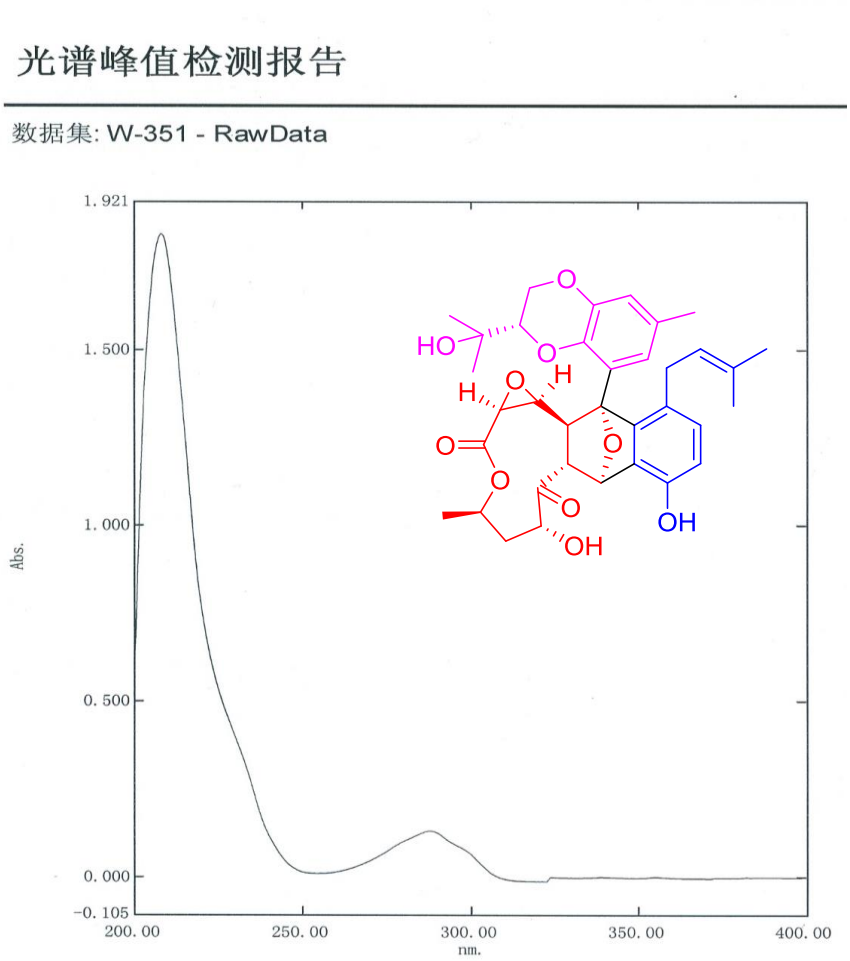

Figure S19. UV spectrum of lithocarpin B (**2**).

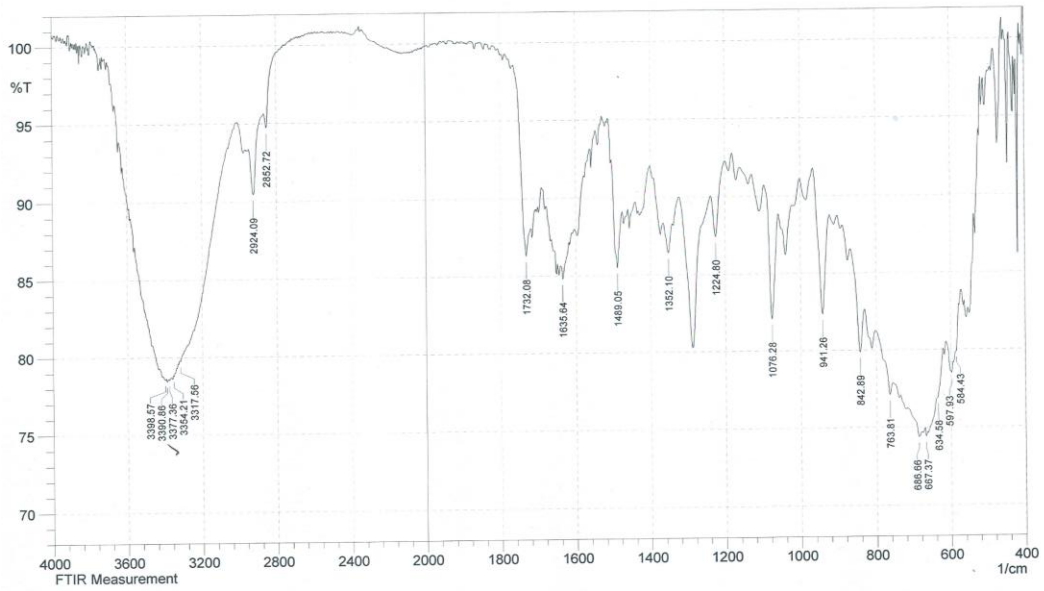

Figure S20. IR spectrum of lithocarpin B (**2**).

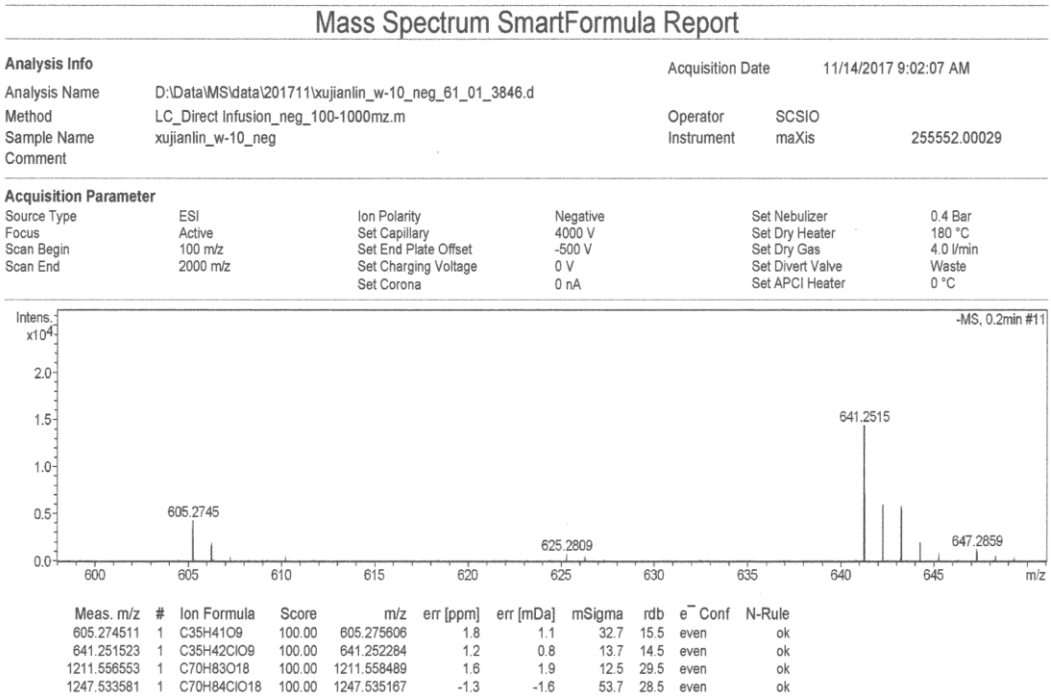

Figure S21. HRESIMS spectrum of lithocarpin C (**3**).

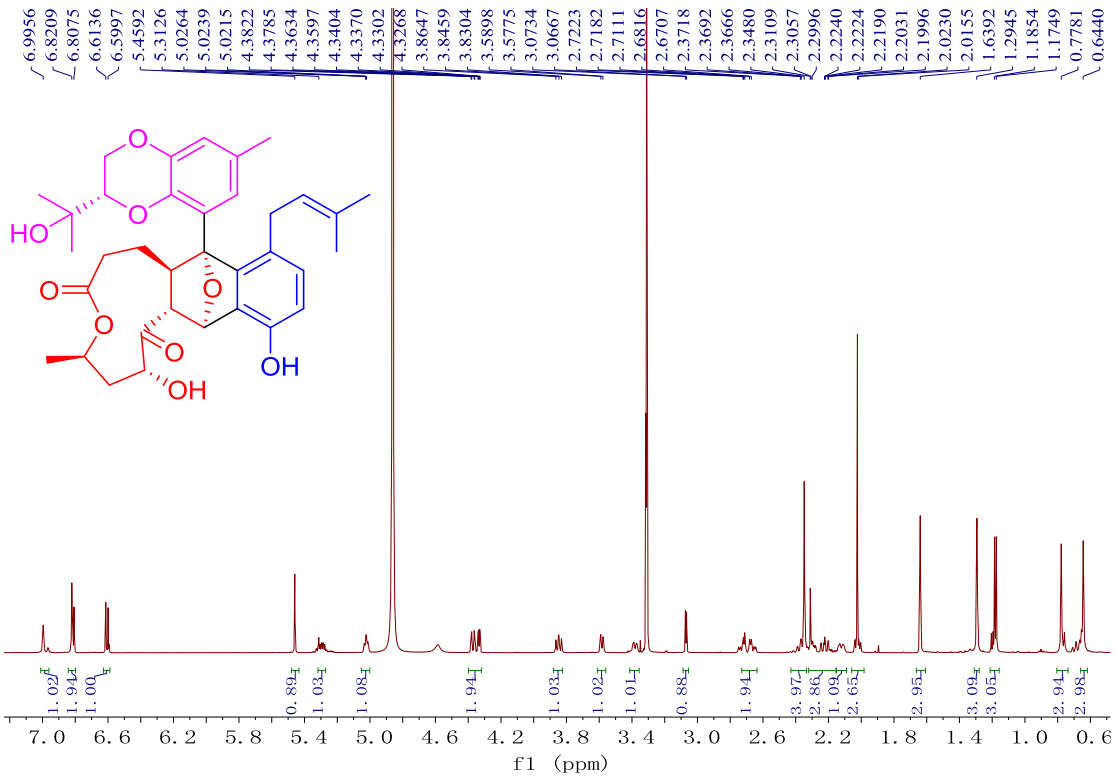

Figure S22. ^{1}H NMR spectrum (500 MHz, CD_3OD) of lithocarpin C (**3**).

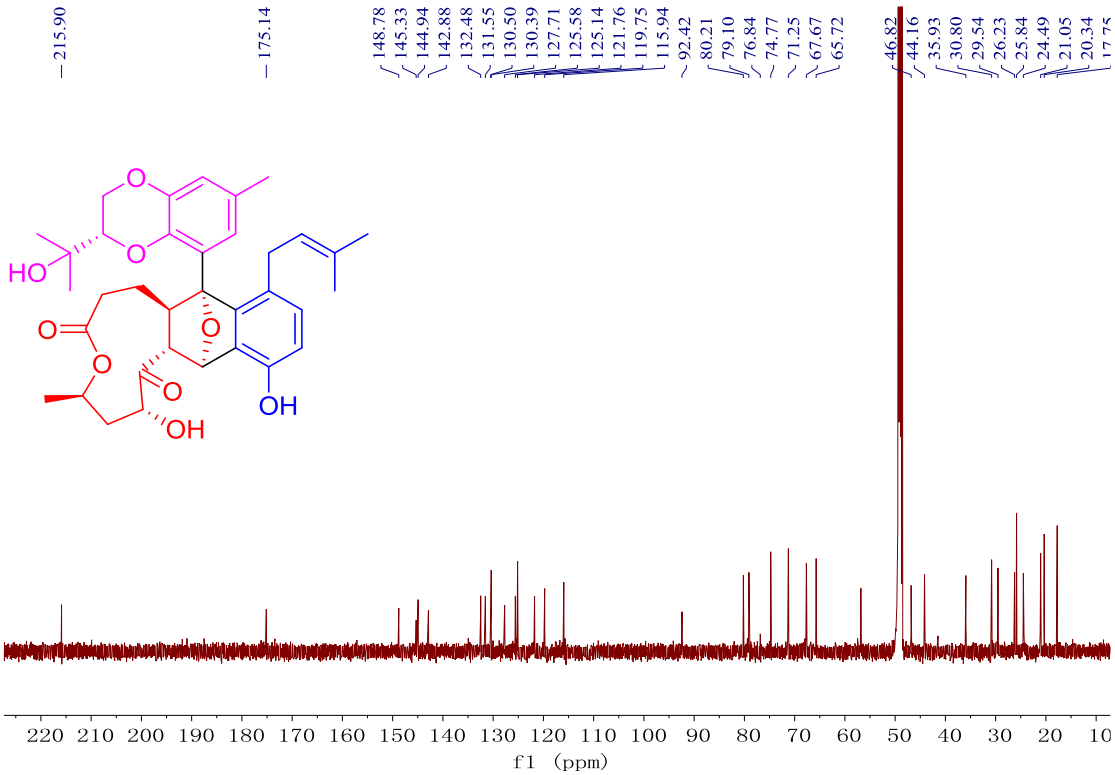

Figure S23. ^{13}C NMR spectrum (125 MHz, CD_3OD) of lithocarpin C (**3**).

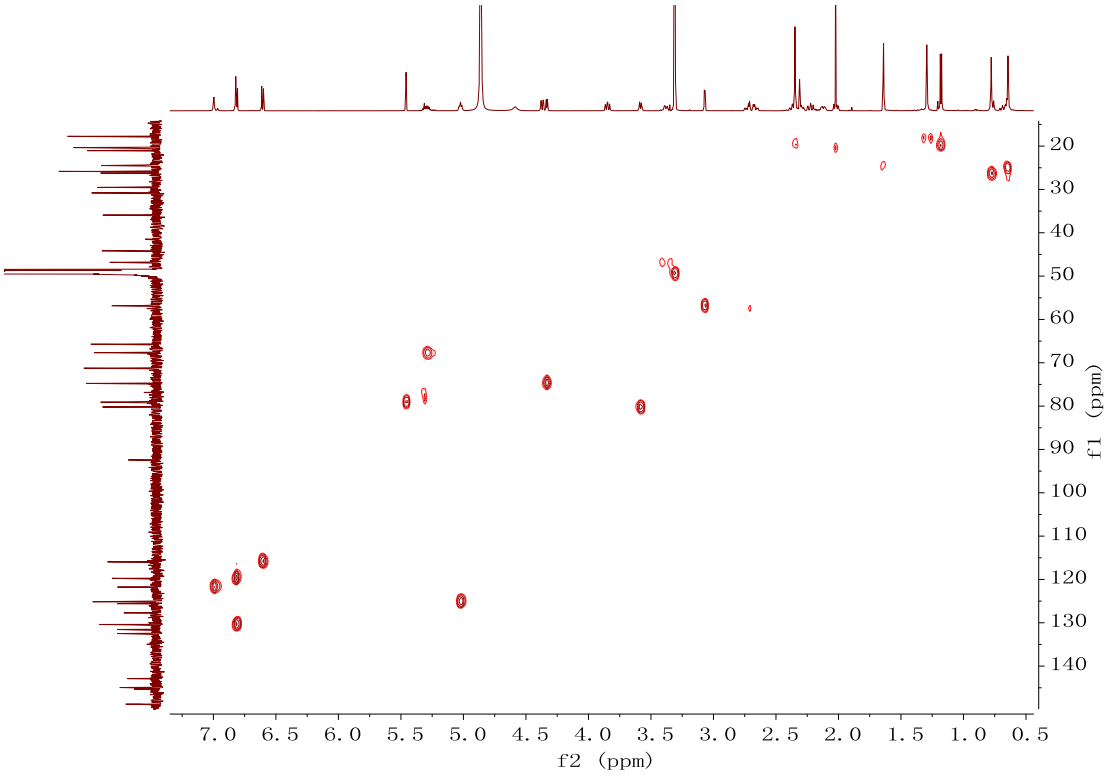

Figure S24. HSQC spectrum of lithocarpin C (**3**).

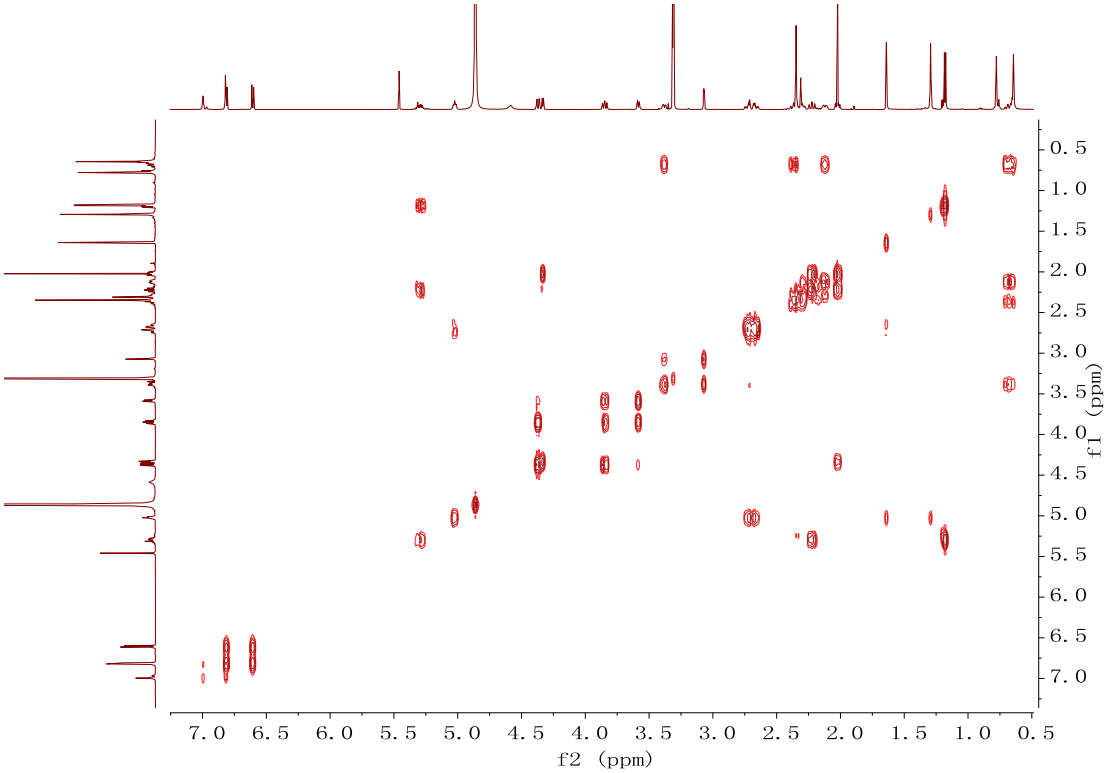

Figure S25. ^{1}H-^{1}H COSY spectrum (500 MHz, CD_3OD) of lithocarpin C (**3**).

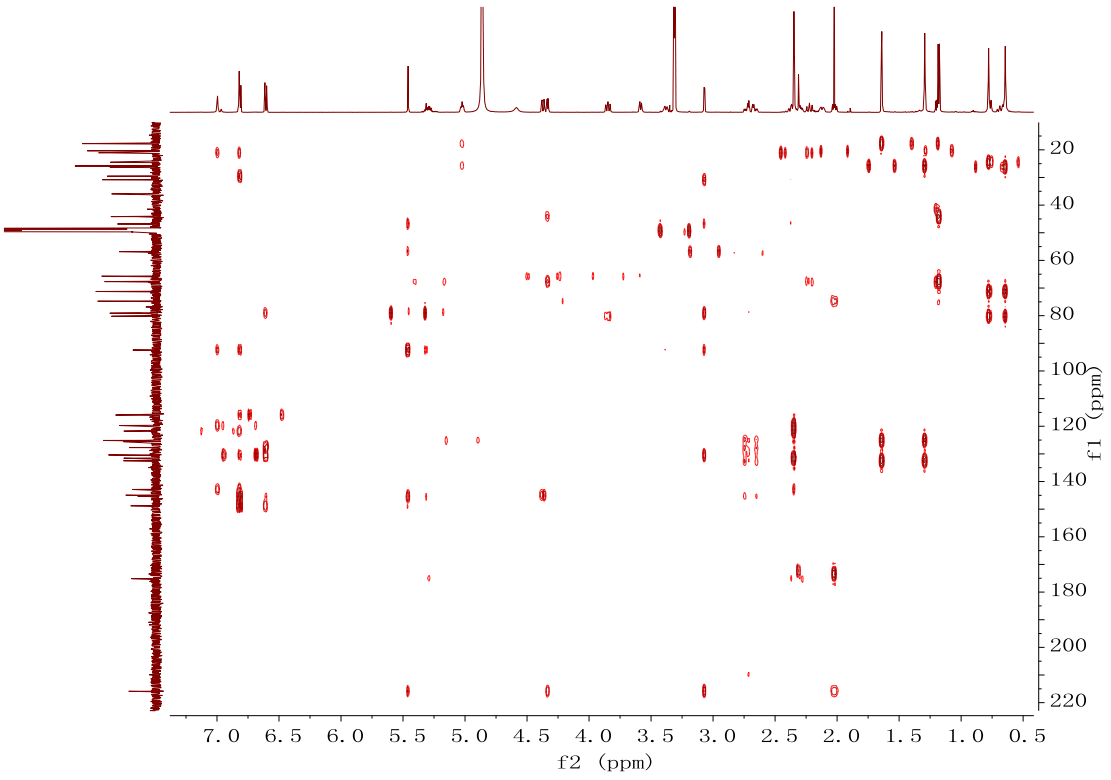

Figure S26. HMBC spectrum of lithocarpin C (**3**).

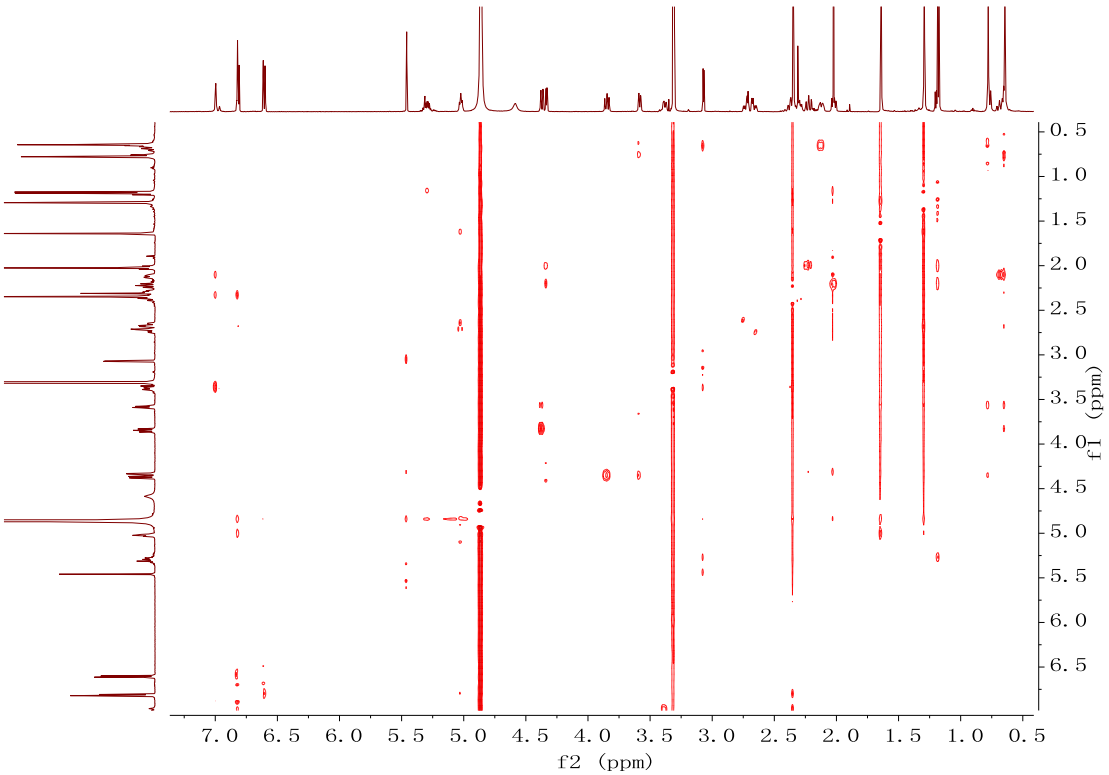

Figure S27. NOESY spectrum (500 MHz, CD_3OD) of lithocarpin C (**3**).

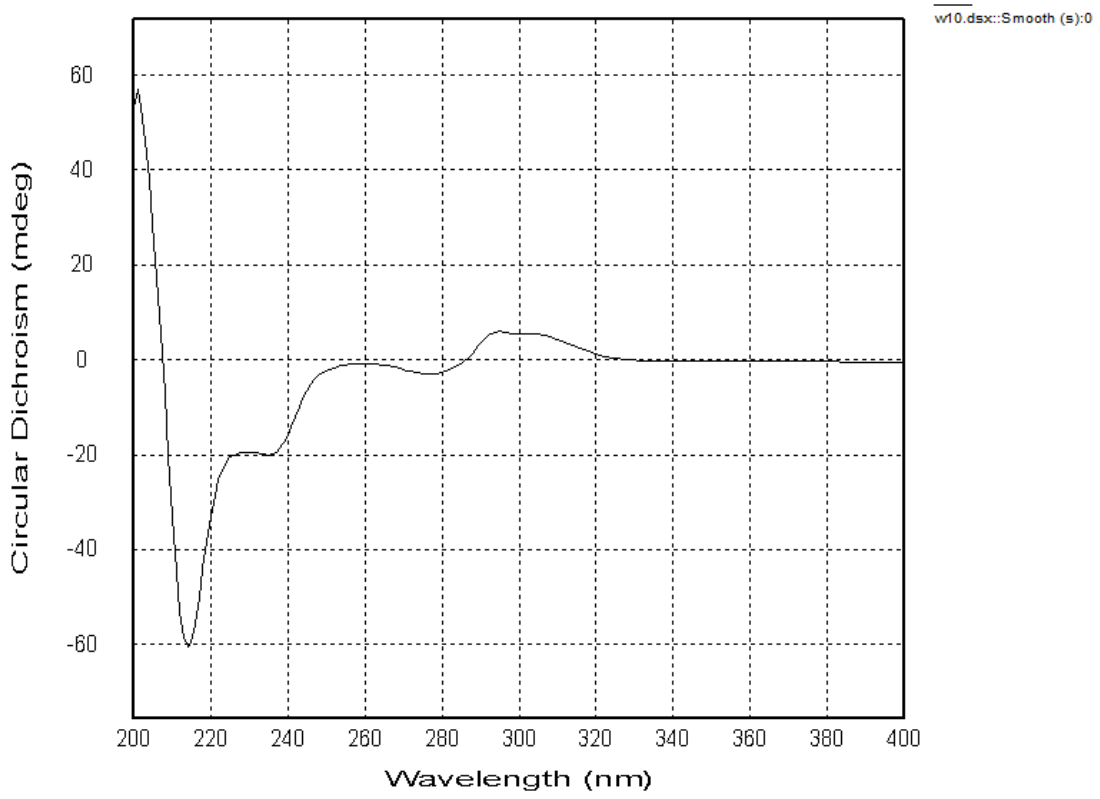

Figure S28. CD spectrum of lithocarpin C (**3**).

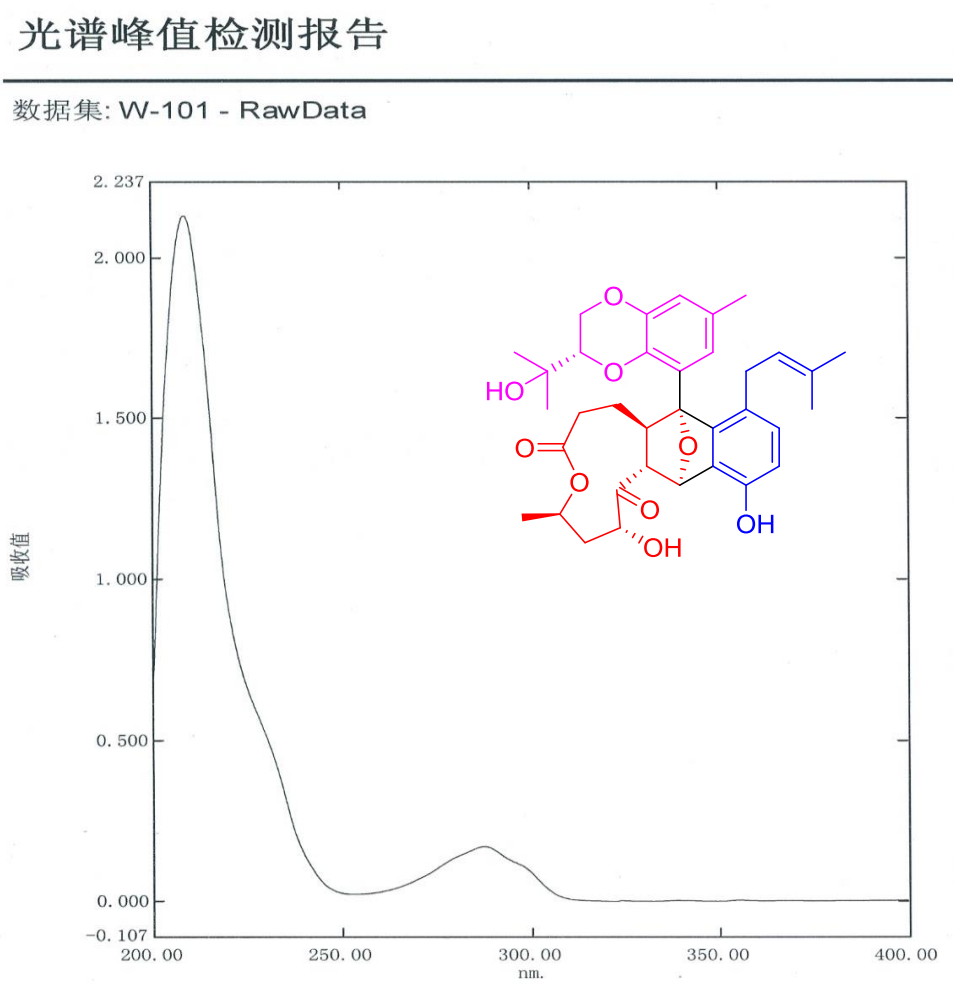

Figure S29. UV spectrum of lithocarpin C (**3**).

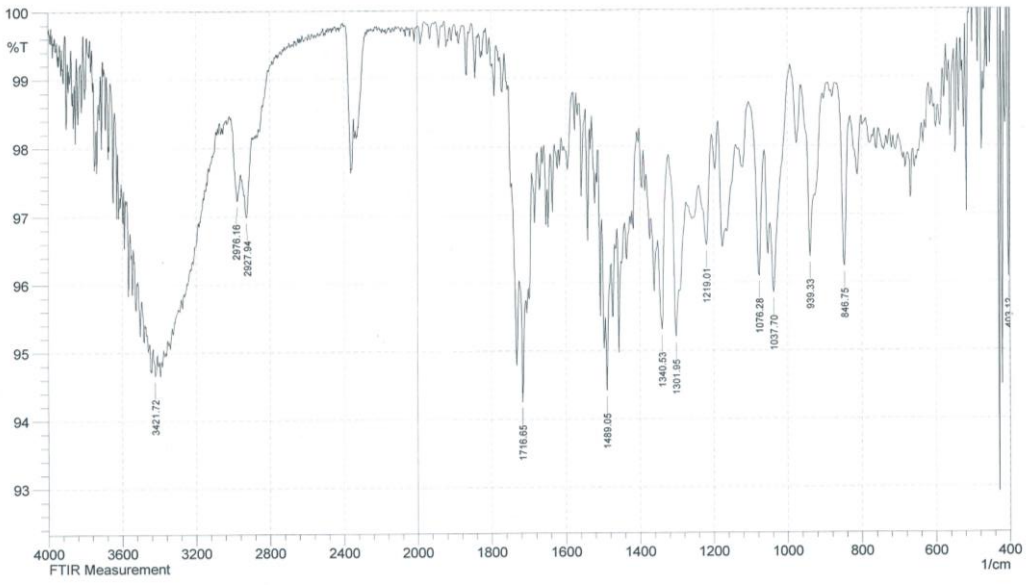

Figure S30. IR spectrum of lithocarpin C (**3**).

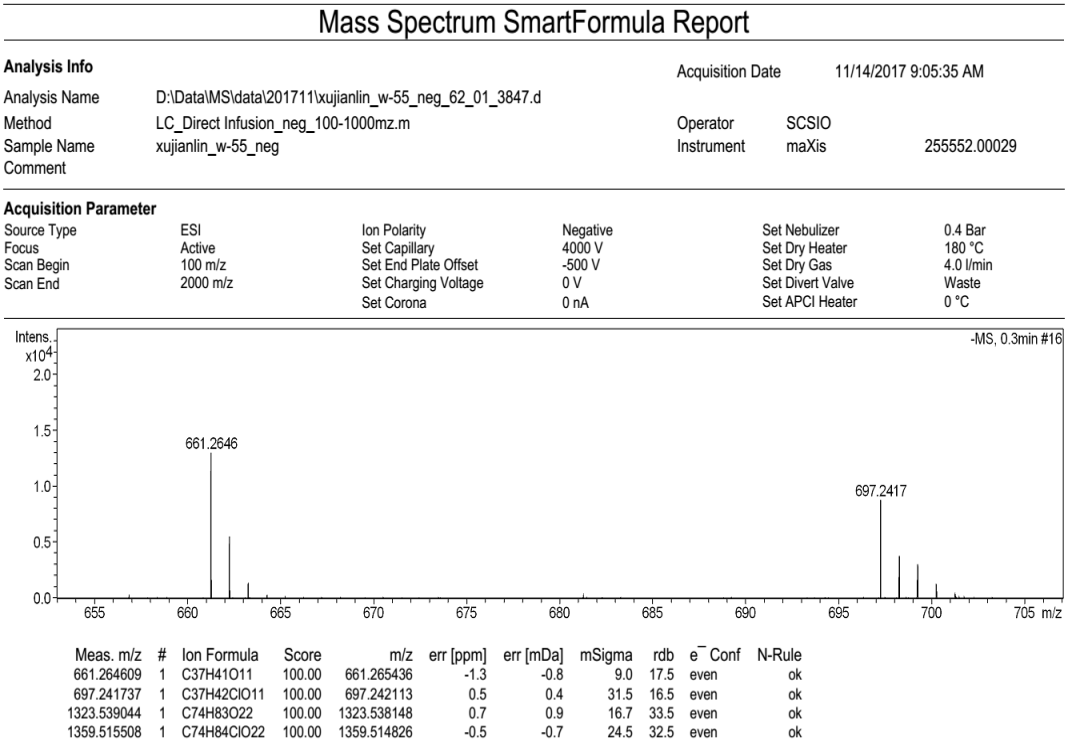

Figure S31. HRESIMS spectrum of lithocarpin D (**4**).

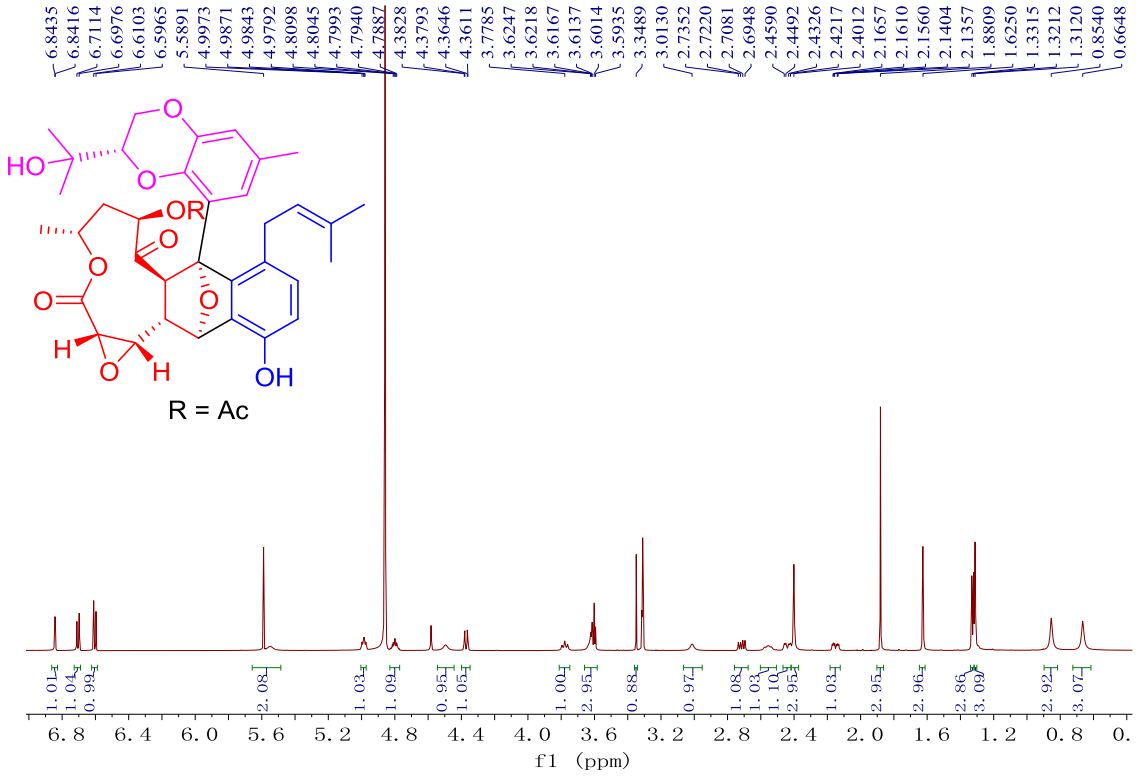

Figure S32. ^{1}H NMR spectrum (500 MHz, CD_3OD) of lithocarpin D (**4**).

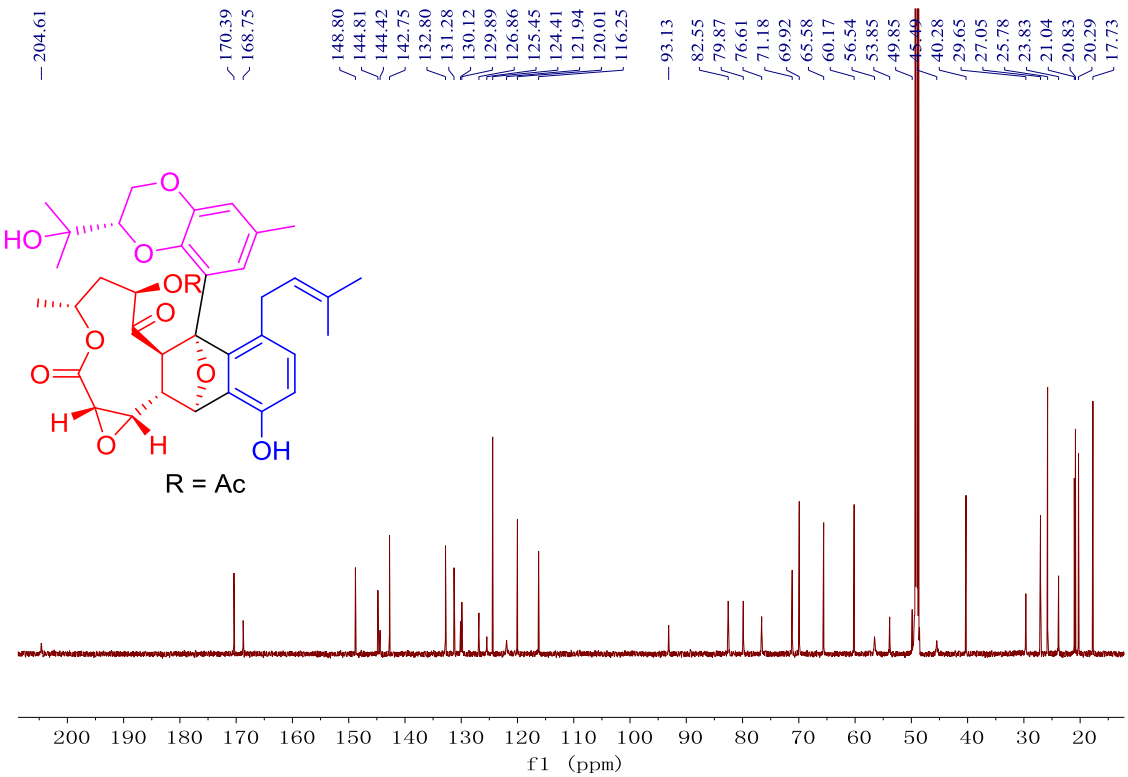

Figure S33. ^{13}C NMR spectrum (125 MHz, CD_3OD) of lithocarpin D (**4**).

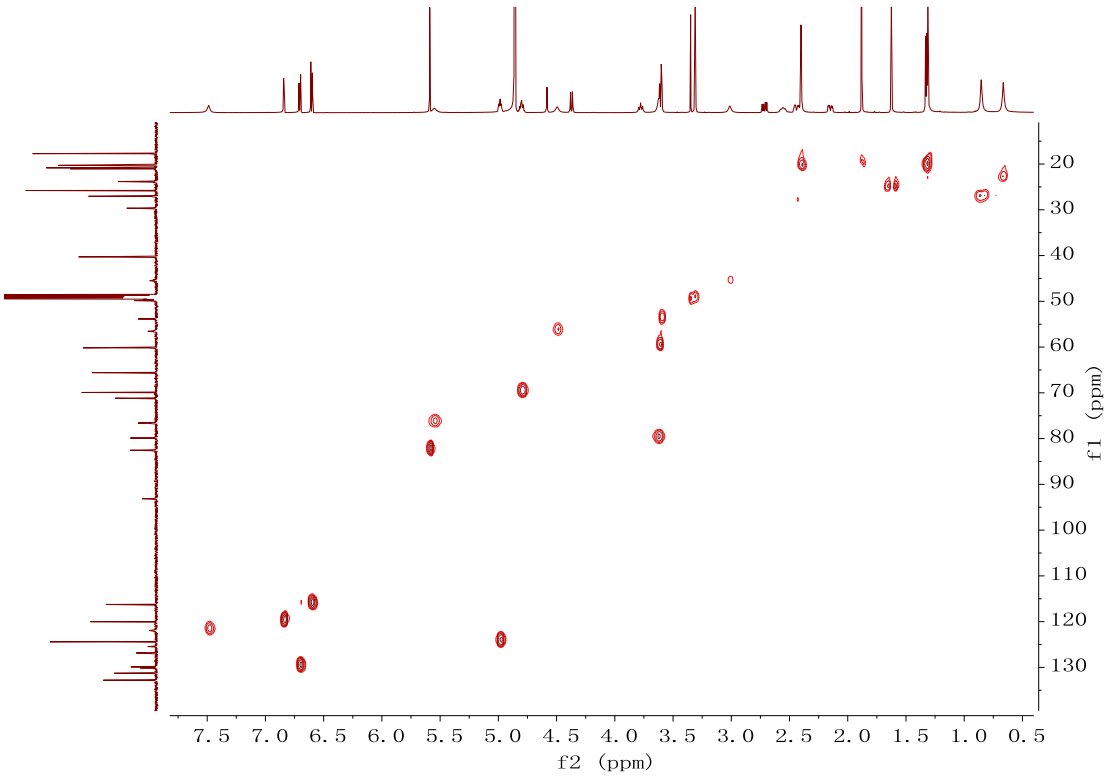

Figure S34. HSQC spectrum of Lithocarpin D (**4**).

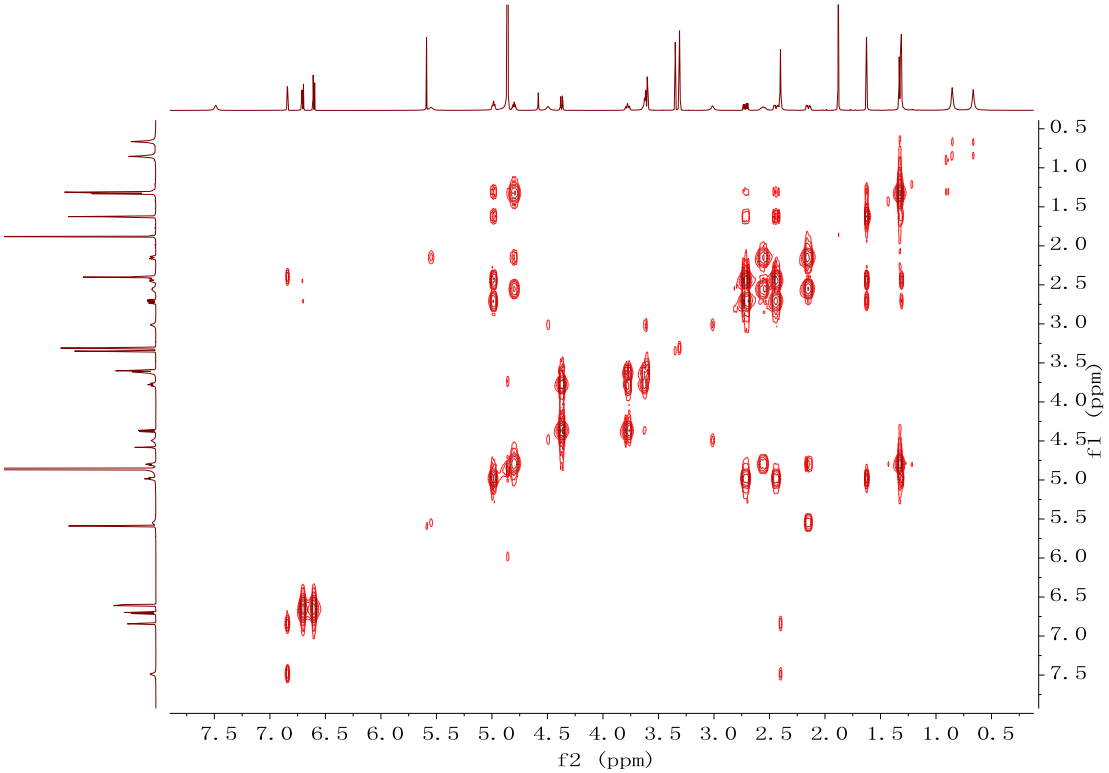

Figure S35. ^{1}H-^{1}H COSY spectrum (500 MHz, CD_3OD) of lithocarpin D (**4**).

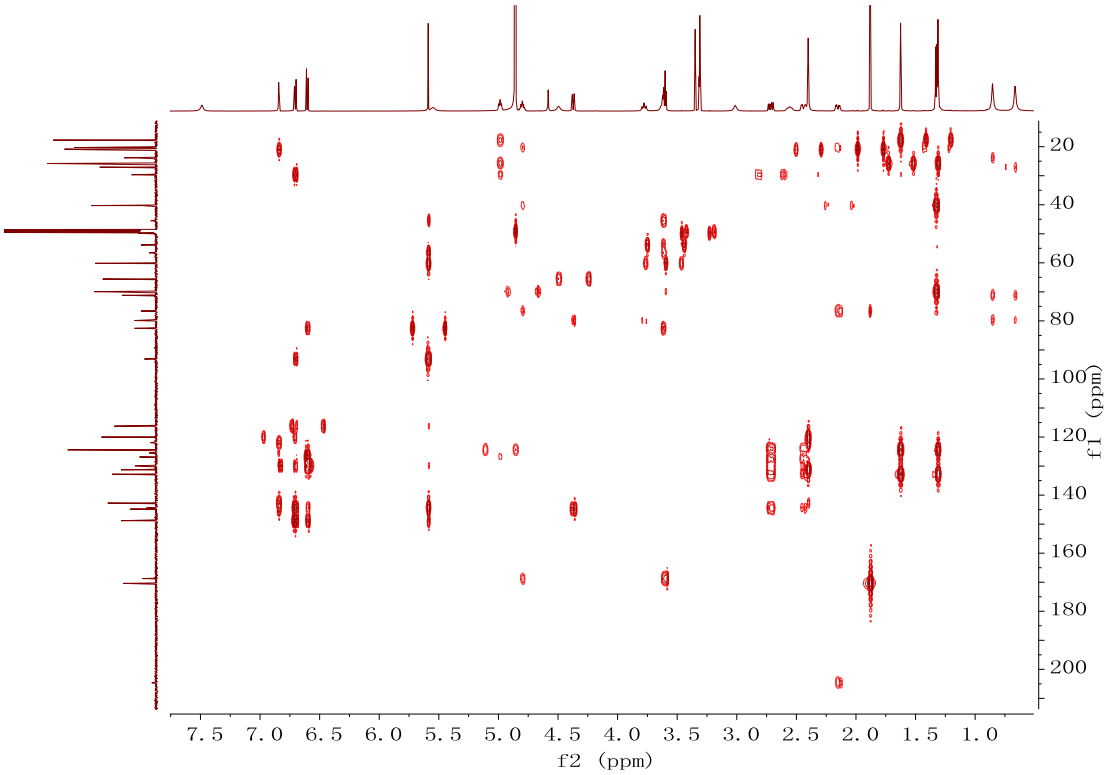

Figure S36. HMBC spectrum of lithocarpin D (**4**).

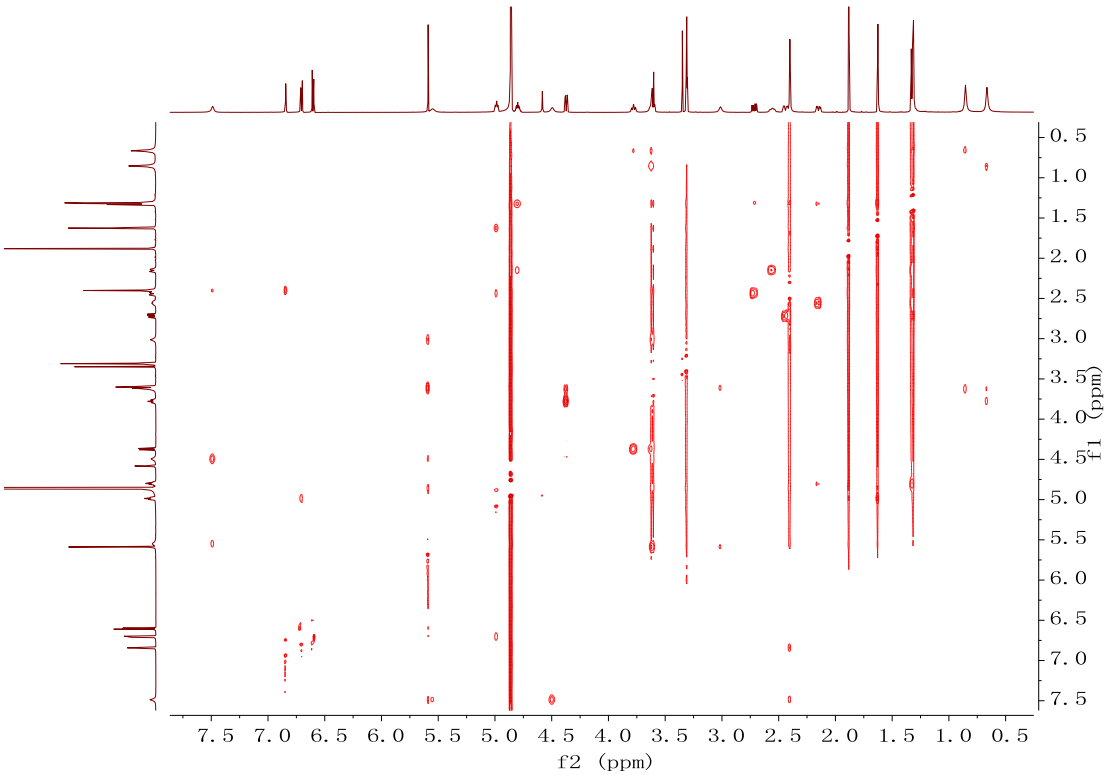

Figure S37. NOESY spectrum (500 MHz, CD_3OD) of lithocarpin D (**4**).

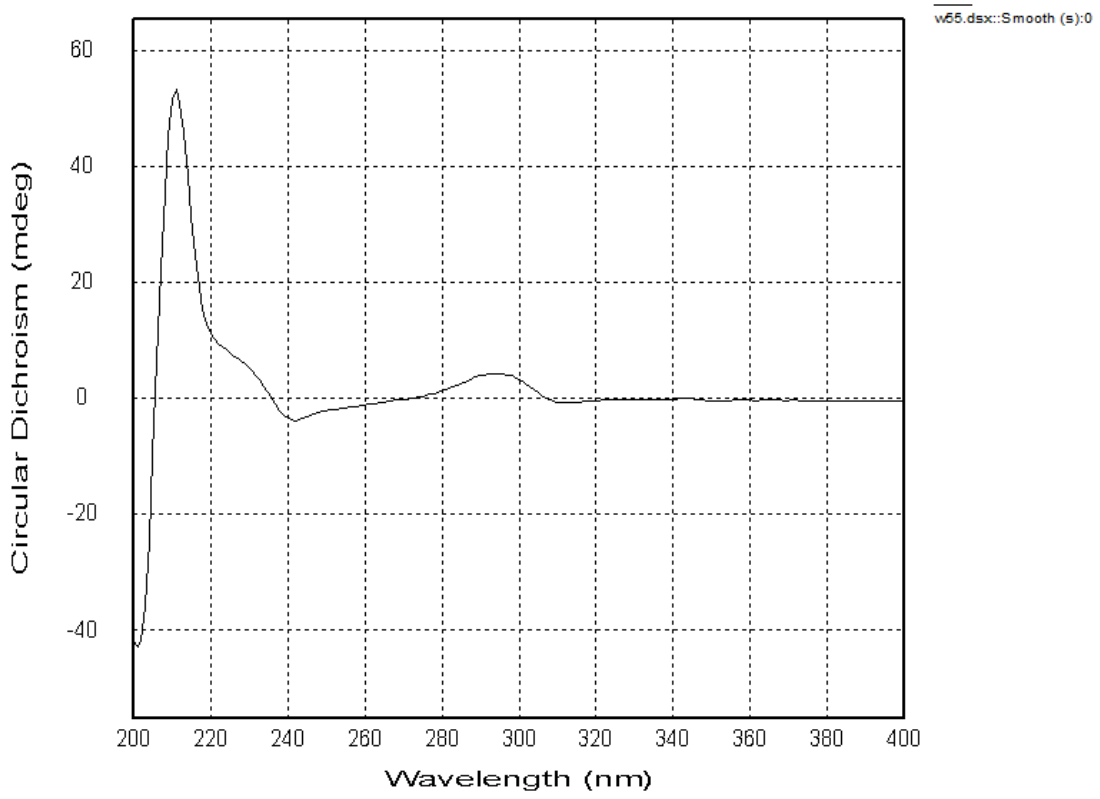

Figure S38. CD spectrum of lithocarpin D (**4**).

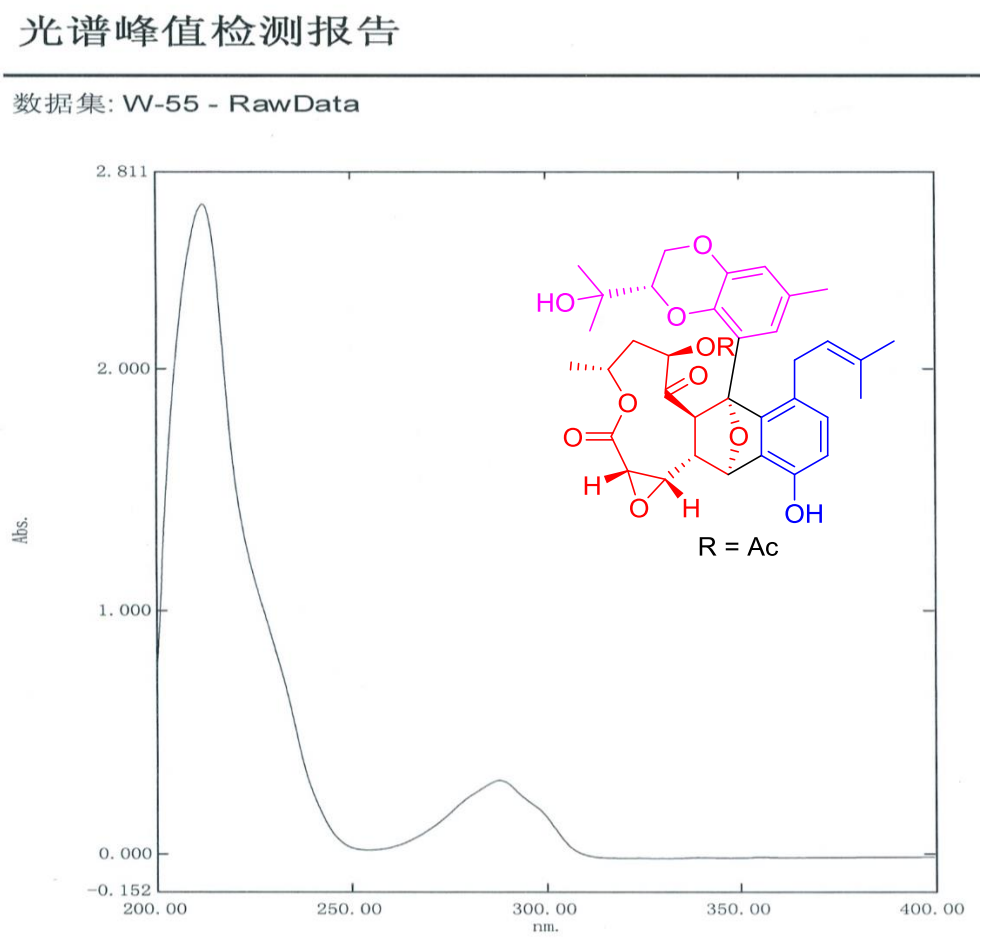

Figure S39. UV spectrum of lithocarpin D (**4**).

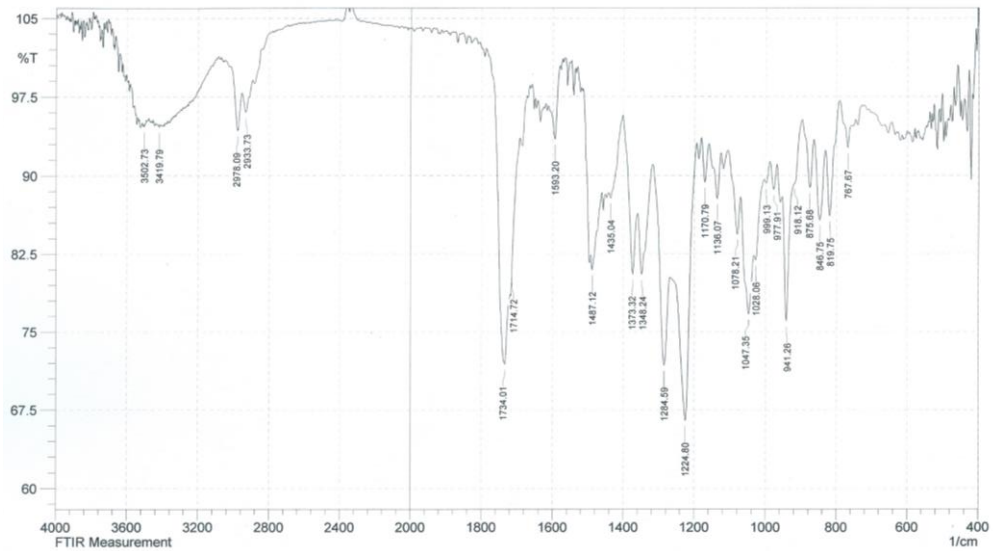

Figure S40. IR spectrum of lithocarpin D (**4**).

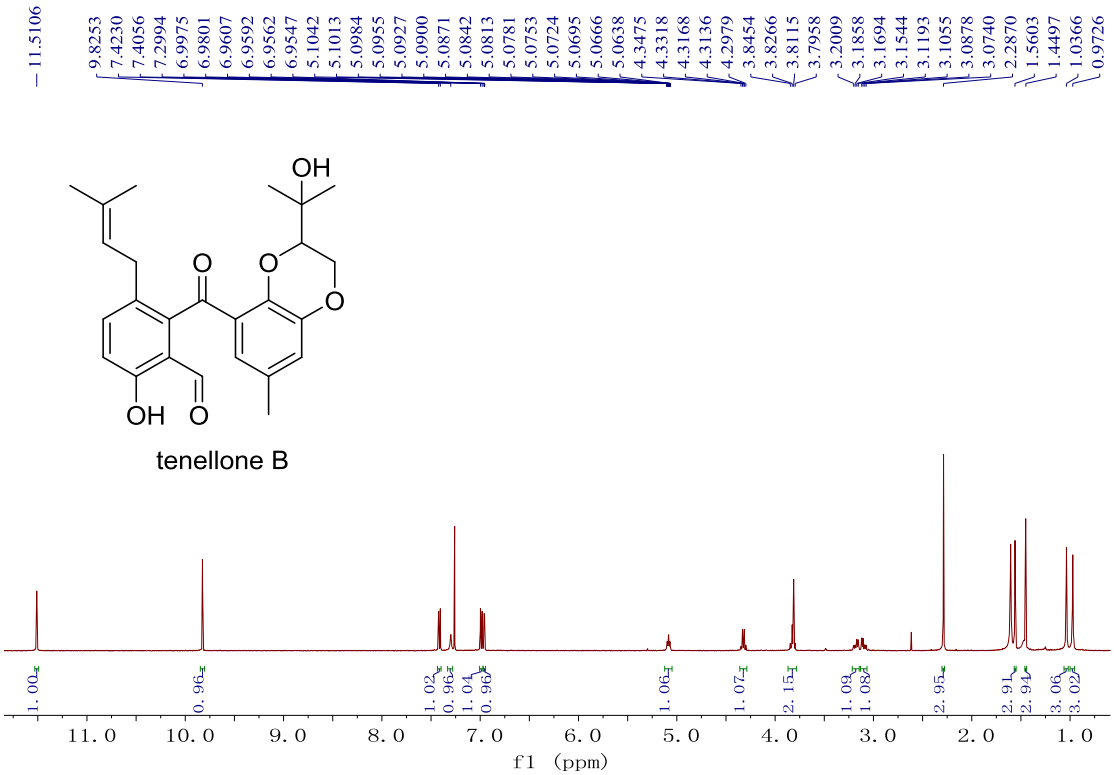

Figure S41. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of tenellone B (**5**).

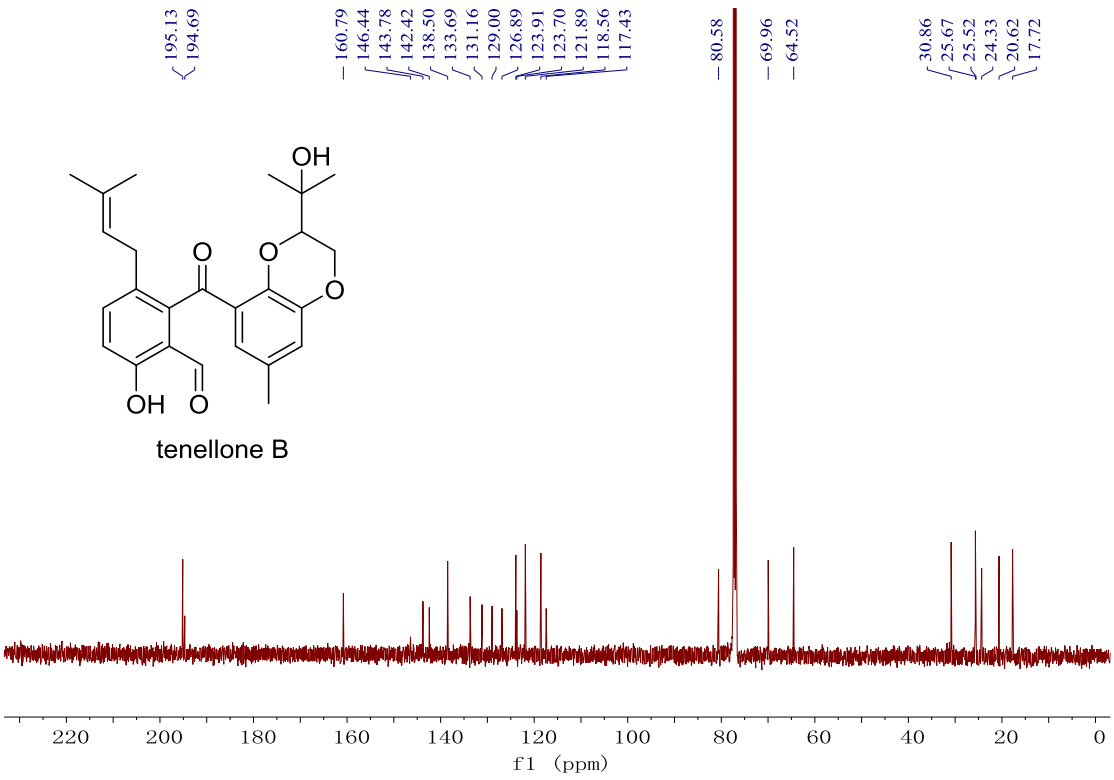

Figure S42. ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of tenellone B (**5**).

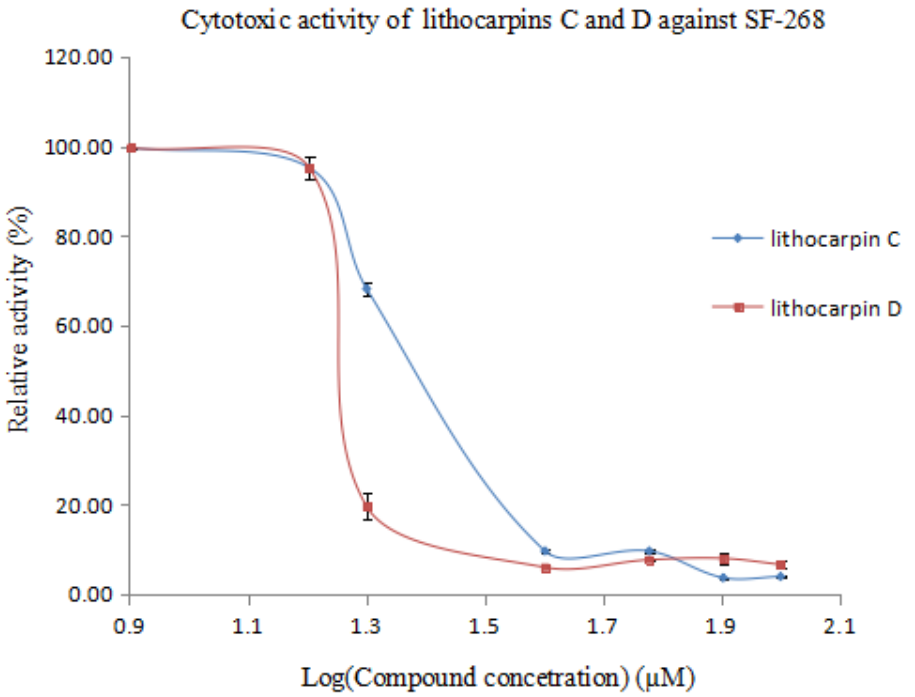

Figure S43. Cytotoxic activity of lithocarpins C and D against SF-268.

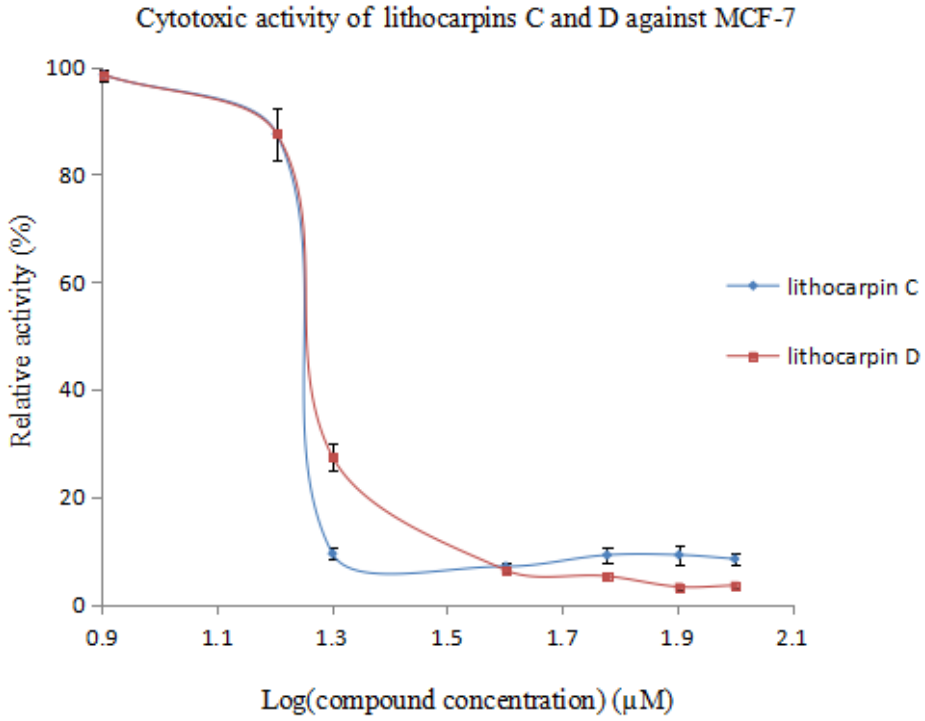

Figure S44. Cytotoxic activity of lithocarpins C and D against MCF-7.

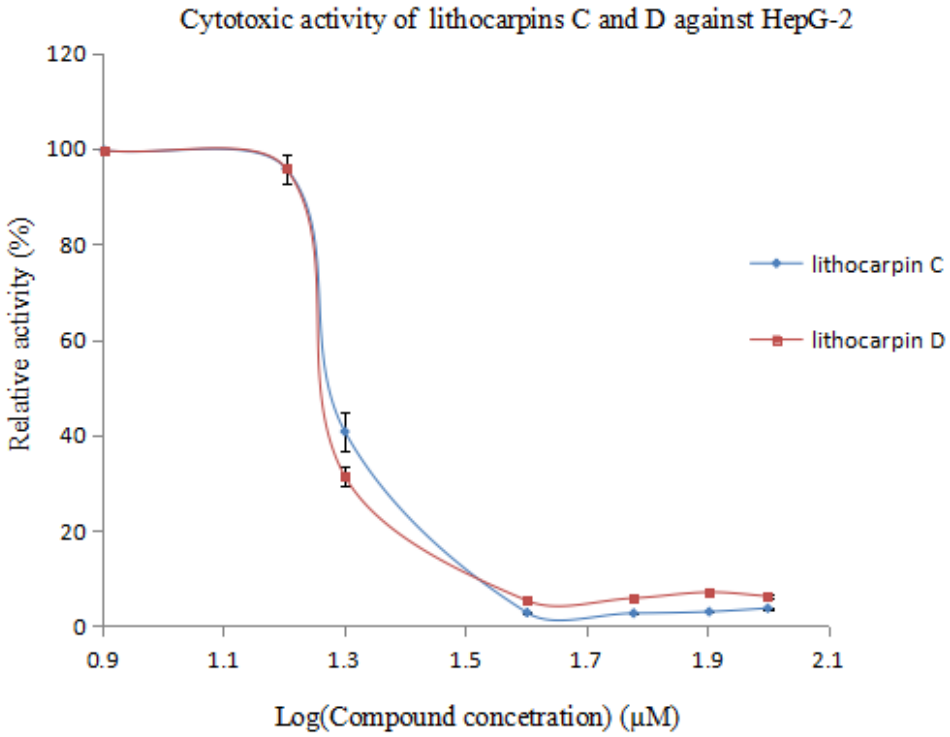

Figure S45. Cytotoxic activity of lithocarpins C and D against HepG-2.