Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Materials

Isochondodendrine and 2′-norcocsuline: additional alkaloids from *Triclisia subcordata,* induced cytotoxicity and Apoptosis on ovarian cancer cell lines

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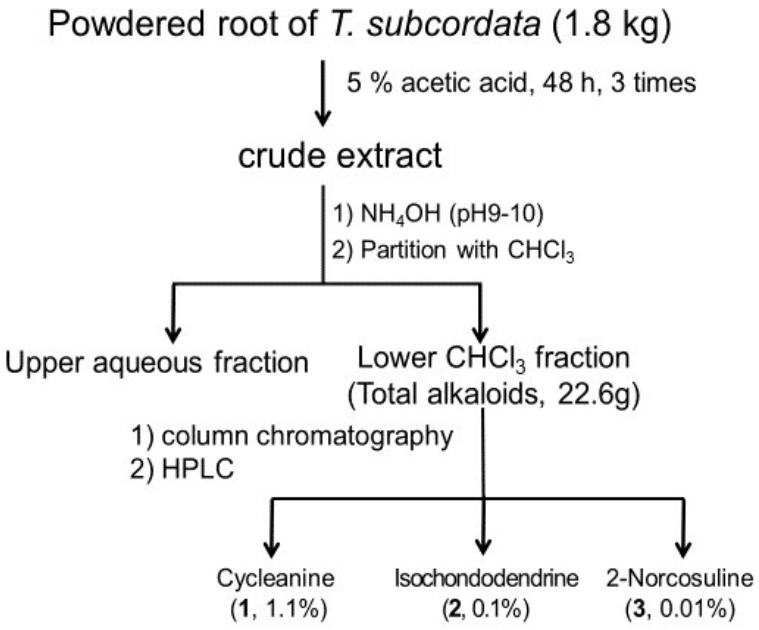

Figure S1 Scheme of extraction by maceration, fractionation, isolation and purification of anti-cancer BBIQ alkaloids from *T. subcordata* root.

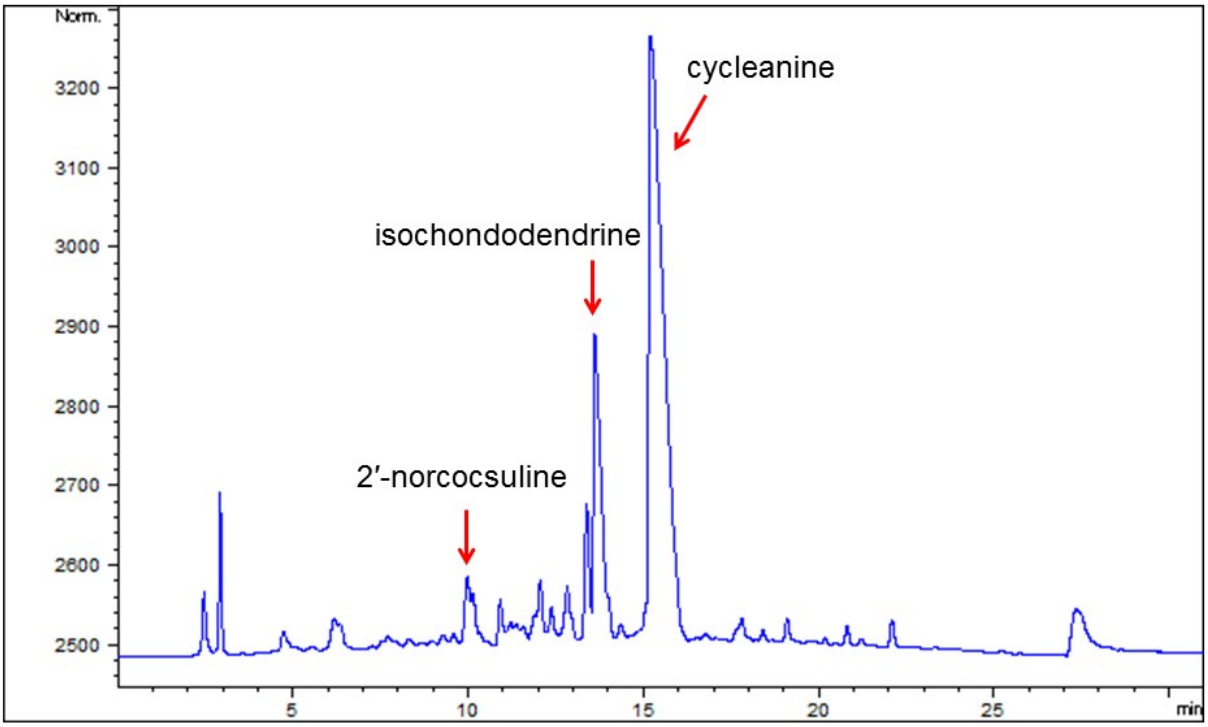

Figure S2. Analytical HPLC chromatogram of the total alkaloids from *T. subcordata* indicating the presence of a major cycleanine, and minor isochondodendrine and 2′-norcocsuline.

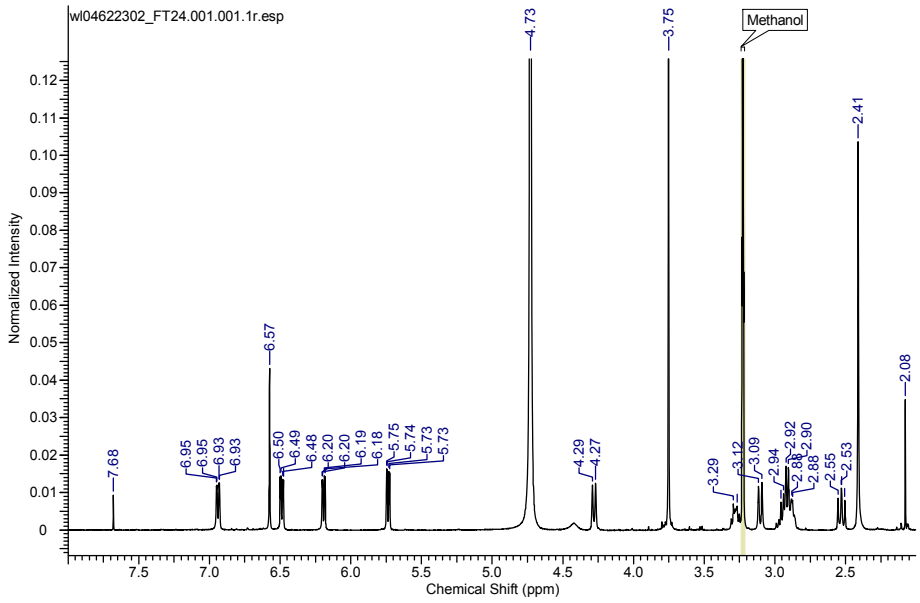

Figure S3 ^{1}H NMR of isochondodendrine (**2**, $CDCl_3$ + CD_3OD (1:1)).

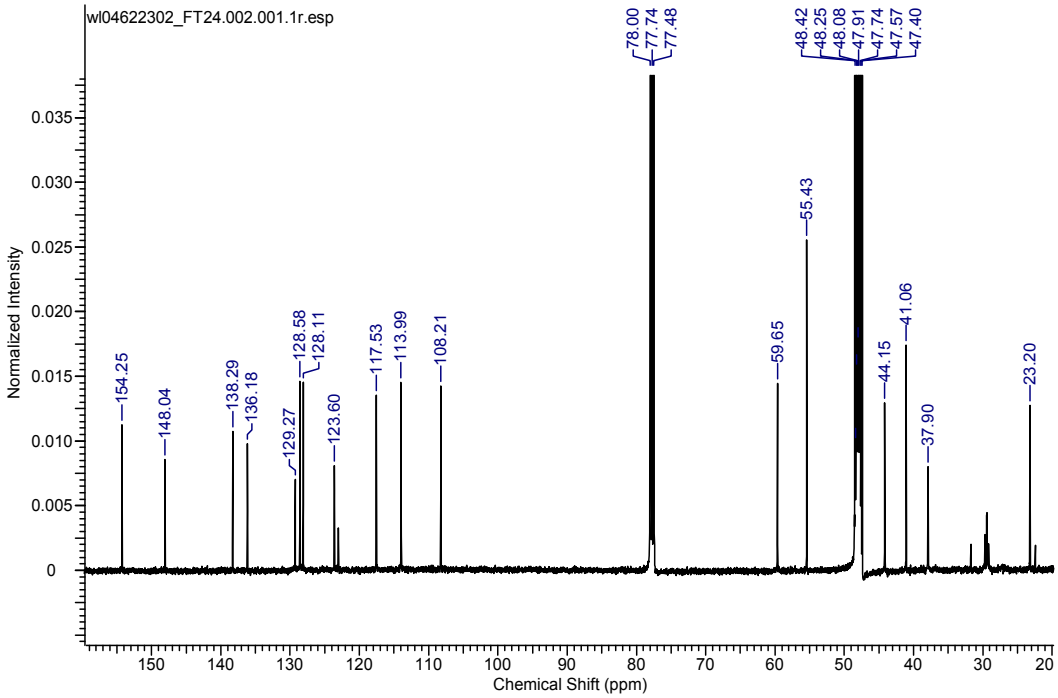

Figure S4 ^{13}C NMR of isochondodendrine (**2**, $CDCl_3$ + CD_3OD (1:1)).

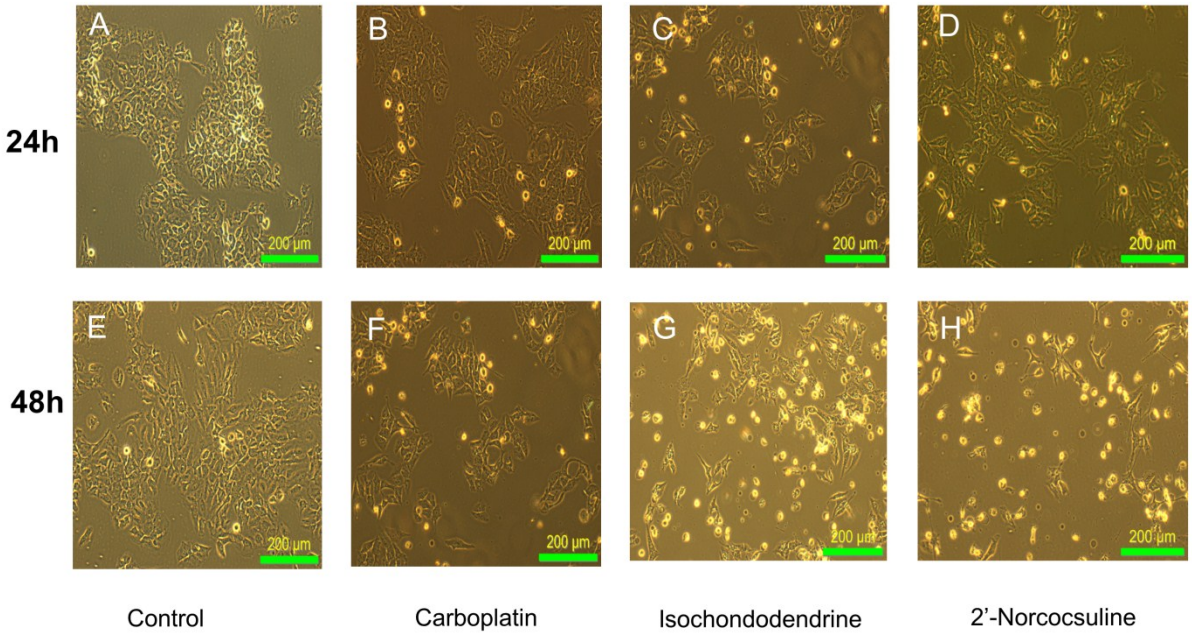

Figure S5 Morphological effects of BBIQ alkaloids on Ovcar-8 cells. Time-dependent effects of control (A and E), carboplatin (B and F), isochondodendrine (C and G); and 2′-norcocsuline (D and H) on the morphology of Ovcar-8 cells. Morphological alterations of Ovcar-8 cells treated with carboplatin, isochondodendrine, and 2′-norcocsuline (20 µM) include membrane blebbing and cell detachment. These effects were reproducible in three independent experiments.

Table S1 ^{1}H NMR (400 MHz) chemical shift data (δ, ppm) for isochondodendrine ($CDCl_3$ + CD_3OD (1:1) (**2**) (J values, in Hz, in parentheses).

Position	Isochondodendrine (2)
H-1	4.28, d (10.7)
H-1′	4.28, d (10.7)
H-3	α, 3.28 m; β, 2.92 m
H-3′	α, 2.92 m; β, 2.92 m
H-4	α, 3.15 m; β, 2.90 m
H-4′	α, 2.92 m; β, 2.92 m
H-5	6.57 s
H-5′	6.57 s
H-10	7.00 (brd)
H-10′	7.00 (brd)
H-11	6.49 dd (8.5; 2.6)
H-11′	6.49 dd (8.5; 2.6)
H-13	5.74 dd (8.5; 2.6)
H-13′	5.74 dd (8.5; 2.6)
H-14	6.19 dd (8.5; 1.5)
H-14′	6.19 dd (8.5; 1.5)
H-α	α, 2.50 m; β, 3.29 m
H-α′	α, 2.50 m; β, 3.27 m
6-OMe	3.75 s
6′-OMe	3.75 s
N-Me	2.41s
N′-Me	2.41s

Table S2 ^{13}C NMR (100 MHz) chemical shift data (δ, ppm) for isochondodendrine (**2**) ($CDCl_3$ + CD_3OD (1:1)).

Carbon	Isochondodendrine (**2**)
1 (1′)	59.65
3 (3′)	44.15
4 (4′)	23.20
4a (4a′)	129.27
5 (5′)	108.21
6 (6′)	148.04
7 (7′)	136.18
8 (8′)	138.29
8a (8a′)	123.60
9 (9′)	128.58
10 (10′)	128.11
11 (11′)	117.53
12 (12′)	154.25
13 (13′)	113.99
14 (14′)	128.11
15 (15′)	37.90
6-OMe (6′-OMe)	55.43
N-Me (N′-Me)	41.06

Table S3. ^{1}H NMR chemical shift data (δ, ppm) for 2′-norcocsuline (**3**) and 2′-norcocsuline-TFA salt (500 MHz, MeOD + $CDCl_3$).

proton	2′-norcocsuline-TFA salt	2′-norcocsuline (**3**)	2′-norcocsuline (**3**) [1]	proton	2′-norcocsuline-TFA salt	2′-norcocsuline (**3**)	2′-norcocsuline (**3**) [1]
H-1	4.32	3.34 m	3.32 m	H-1′	4.78	4.36 brs	4.35 brs
H-3	3.15, 3.07	2.65 m	2.67 m;	H-3′	3.05, 3.23	2.86 m;	2.86 m;
						3.33 m	3.17 m
H-4	3.12, 2.95	2.65 m	2.67 m;	H-4′	2.95,3.12		
H-5	6.62s	6.63 s	6.62 s	H-5′	6.69 s	6.33 s	6.31 s
H-8	6.51s	6.17 s	6.15 s	H-8′	-		
H-15	3.67, 3.56	2.72 m;	2.67 m;	H-15′	3.32, 3.12	3.15 m;	2.62 m;
		2.98 dd	2.95 dd (14.2, 2.0)			3.27 dd	3.32 dd (15.0, 2.3)
H-10	6.88 d	6.53 (d, 1.9)	6.50 brs	H-10′	7.12	7.20 dd (7.9, 2.1)	7.19 brd
H-11	-			H-11′	6.91	6.97 (dd, 8.2, 2.5)	7.00 (dd, 8.2, 2.4)
H-13	6.84d	6.93 d (8.2)	6.91 d (8.1)	H-13′	7.23	7.22 (dd, 8.2, 2.4)	7.2 brd
						7.17	
H-14	6.90 dd	6.85 dd (8.0; 1.6)	6.82 dd (8.1; 1.6)	H-14′	7.59 brd	7.68 (dd, 8.4, 1.3)	7.7 brd
N-Me	2.53 (brs)	2.46 s	2.44 s	6′-OMe	3.86 s	3.88 s	3.86 s

Table S4 ^{13}C NMR (125 MHz, CD_3OD (48.0 ppm as reference) + $CDCl_3$) chemical shift data (δ, ppm) for 2′-norcocsuline (**3**) and the 2′-norcosculine-TFA salt.

Carbon	2′-norcocsuline-TFA salt	2′-norcocsuline (**3**)	2′-norcocsuline [1]	Carbon	2′-norcocsuline-TFA salt	2′-norcocsuline (**3**)	2′-norcocsuline [1]
1	62.8	67.4	67.5	1′	51.8	54.0	54.2
3	47.5	49.3	49.6	3′	40.0	44.6	44.9
4	23.6	27.7	27.7	4′	23.1	27.7	28.3
4a	131.2	-	134.8	4a′	129.7	-	129.8
5	118.4	115.4	115.5	5′	107.9	106.3	106.7
6	138.5	-	139.5	6′	146.2	-	146.1
7	139.8	-	139.7	7′	130.6	-	135.7
8	114.4	113.8	114.1	8′	138.5	-	140.6
8a		-	133.8	8a′	121.5	-	122.0
15	36.1	40.7	41.3	15′	40.2	38.4	38.7
9	126.5	-	129.6	9′	139.9	-	138.9
10	116.1	116.2	116.6	10′	130.8	-	131.3
11	146.2	-	143.7	11′	123.0	121.2	121.3
12	148.3	-	148.1	12′	161.7	-	153.9
13	115.9	115.3	115.8	13′	122.4	122.4	122.5
14	116.8	122.4	122.2	14′	130.0	128.2	128.2
N-Me	35.4	42.4	43.0	6′-OMe	55.7	56.1	56.3

-, peaks are not observed due to dilute sample in ^{13}C NMR recording.

Reference

[1] Liu Y, Harinantenaina L, Brodie PJ, Slebodnick C, Callmander MW, Rakotondrajaona R, Rakotobe E, Rasamison VE, TenDyke K, Shen Y. Structure elucidation of antiproliferative bisbenzylisoquinoline alkaloids from Anisocycla grandidieri from the Madagascar dry forest. *Magn Reson Chem.* **2013,** 51, 574-579