Supporting Information

(−)-Neocaryachine, An Antiproliferative Pavine Alkaloid from *Cryptocarya laevigata* Induces DNA Double-strand Breaks

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Table S1. Human tumor cell line assay data for the crude organic extract of *L. corymbulosa*.

Alkaloids	Cell lines[a] /IC_{50} (μM)[b]				
	A549	MDA-MB-231	MCF-7	KB	KB-VIN
N025183	0.25	0.23	0.49	0.64	0.37
PXL (nM)	6.20	8.82	10.40	6.27	1926

[a]A549 (lung carcinoma), MDA-MB-231 (triple-negative breast cancer), MCF-7 (estrogen receptor-positive & HER2-negative breast cancer), KB (epidermoid carcinoma of the nasopharynx), KB-VIN (P-gp-overexpressing MDR subline of KB). [b] Antiproliferative activity as IC_{50} values for each cell line, the concentration of compound that caused 50% reduction relative to untreated cells determined by the SRB assay.

Characterizations of all isolated alkaloids from the bark of *Cryptocarya laevigata*

*(−)-Neocaryachine (**1**).* $[\alpha]^{26}_{D}$ −199 (*c* 0.05, MeOH); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 2.53 (s, 3H, N-CH_3), 2.59 (d, *J* =16.1 Hz, 1H, H-11β), 2.72 (d, *J* =16.5 Hz, 1H, H-5β), 3.31 (dd, *J* =16.5, 5.8 Hz, 1H, H-5α), 3.37 (dd, *J* =16.1, 5.7 Hz, 1H, H-11α), 3.83 (s, 3H, 8-OMe), 3.98 (d, *J* =5.7 Hz, 1H, H-12), 4.34 (d, *J* =5.8 Hz, 1H, H-6), 5.69 (brs, 1H, 7-OH), 5.80 (d, *J* =1.4 Hz, 1H, 2,3-OCH_2O-), 5.85 (d, *J* =1.4 Hz, 1H, 2,3-OCH_2O-), 6.43 (s, 1H, H-4), 6.50 (d, *J* =8.1 Hz, 1H, H-10), 6.58 (s, 1H, H-1), 6.66 (d, *J* =8.1 Hz, 1H, H-9); ^{13}C-NMR ($CDCl_3$, 150 MHz) : δ 31.6 (C-5), 33.0 (C-11), 40.9 (N-CH_3), 51.6 (C-6), 56.2 (8-OMe), 56.8 (C-12), 100. 6 (2,3-OCH_2O-), 107.2 (C-1), 108.9 (C-4), 109.3 (C-9), 119.7 (C-10), 124.5 (C-6a), 125.4 (C-10a), 126.3 (C-4a), 130.0 (C-12a), 142.0 (C-7), 144.3 (C-8), 145.9 (C-2), 146.3 (C-3); HRMS *m/z* 326.1412 $[M+H]^+$

*(−)-Isocaryachine (**2**).* $[\alpha]^{29}_{D}$ −201.9 (*c* 0.34, EtOH); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 2.51 (s, 3H, N-CH_3), 2.52 (d, *J* =16.4 Hz, 1H, H-11β), 2.55 (d, *J* =17.0 Hz, 1H, H-5β), 3.34 (dd, *J* =16.4, 5.8 Hz, 1H, H-11α), 3.38 (dd, *J* =17.0, 5.8 Hz, 1H, H-5α), 3.85 (s, 3H, 8-OMe), 3.96 (d, *J* =5.8 Hz, 2H, H-6, 12), 5.47 (brs, 1H, 9-OH), 5.81 (d, *J* =1.5 Hz, 1H, 2, 3-OCH_2O), 5.86 (d, *J* =1.5 Hz, 1H, 2, 3-OCH_2O-), 6.41 (s, 1H, H-4), 6.51 (s, 1H, H-10), 6.57 (s, 1H, H-7), 6.58 (s, 1H, H-1); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ33.3 (C-11), 34.6 (C-5), 41.0 (N-CH_3), 56.1 (C-6), 56.5 (8-OMe), 56.9 (C-12), 100.7 (2, 3-OCH_2O-), 107.2 (C-1), 108.8 (C-4), 109.4 (C-7),

114.5 (C-10), 124.8 (C-10a), 125.1 (C-4a), 129.5 (C-6a), 131.4 (C-12a), 144.5 (C-9), 145.3 (C-8), 146.1 (C-2), 146.4 (C-3) FABMS *m/z* 326.193 $[M+H]^+$

*(–)-Crychine (**3**).* $[\alpha]^{27}_D$ −214.9 (*c* 2.98, EtOH); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ2.50 (s, 3H, N-CH_3), 2.53 (d, *J* =16.4 Hz, 2H, H-5β, H-11β), 3.35 (dd, *J* =16.4, 5.8 Hz, 2H, H-5α, H-11α), 3.94 (d, *J* =5.8 Hz, 2H, H-6, H-12), 5.80 (d, *J* =1.5 Hz, 2H, 2,3-OCH_2O-, 8,9-OCH_2O-), 5.85 (d, *J* =1.5 Hz, 2H, 2,3-OCH_2O-, 8,9-OCH_2O-), 6.41 (s, 2H, H-4, H-10), 6.57 (s, 2H, H-1, H-7); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ 34.1 (C-5, C-11), 40.9 (N-CH_3), 56.7 (C-6, C-12), 100.7 (2,3-OCH_2O-, 8,9-OCH_2O-), 107.1 (C-1, C-7), 108.7 (C-4, C-10), 125.0 (C-4a, C-10a), 131.0 (C-6a, C-12a), 146.1 (C-2, C-8), 146.4 (C-3, C-9); FABMS *m/z* 324.089 $[M+H]^+$

*(–)-Eschscholtzine-N-oxide (**4**).* $[\alpha]^{28}_D$ −26.0 (*c* 0.14, MeOH); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ2.68 (d, *J* =16.1 Hz, 1H, H-11β), 3.05 (d, *J* =17.4 Hz, 1H, H-5β), 3.37 (s, 3H, N-CH_3), 3.51 (dd, *J* =17.4, 5.8 Hz, 1H, H-5α), 4.20 (dd, *J* =16.1, 5.3 Hz, 1H, H-11α), 4.46 (d, *J* =5.3 Hz, 1H, H-12), 4.54 (d, *J* =5.8 Hz, 1H, H-6), 5.87 (s, 2H, 8, 9-OCH_2O-), 5.90 (d, *J* =1.4 Hz, 1H, 2, 3-OCH_2O-), 5.94 (d, *J* =1.4 Hz, 1H, 2, 3-OCH_2O-), 6.48 (s, 1H, H-4), 6.50 (s, 1H, H-10), 6.57 (s, 1H, H-7), 6.63 (s, 1H, H-1); FABMS *m/z* 340.181 $[M+H]^+$

*(–)-Norargemonine (**5**).* $[\alpha]^{28}_D$ −159.6 (*c* 0.01, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 2.52 (s, 3H, N-CH_3), 2.57 (dd, *J* =16.7, 5.5 Hz, 2H, H-5β/H-11β), 3.30–3.50 (m, 2H, H-5α/H-11α), 3.78 (s, 3H, 3-OCH_3), 3.77 and 3.78 (each s, 3H, 3-OCH_3/9-OCH_3), 3.84 (s, 3H, 2-OCH_3), 3.98 (t, *J* =5.5 Hz, 2H, H-6/H-12), 5.41 (s, 1H, 8-OH), 6.42 and 6.43 (each s, 1H, H-4/H-10), 6.60 (s, 1H, H-1), 6.68 (s, 1H, H-7); FABMS *m/z* 342.208 $[M+H]^+$

*(–)-Bisnorargemonine (**6**).* $[\alpha]^{28}_D$ −54.1 (*c* 0.025, MeOH); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 2.51 (s, 3H, N-CH_3), 2.54 (d, *J* =15.0 Hz, 1H, H-11β), 2.56 (d, *J* =14.2 Hz, 1H, H-5β), 3.34 (dd, *J* =15.0, 5.8 Hz, 1H, H-11α), 3.39 (dd, *J* =14.2, 6.1 Hz, 1H, H-5α), 3.78 (s, 3H, 3-OCH_3), 3.85 (s, 3H, 8-OCH_3), 3.96 (d, *J* =5.8 Hz, 1H, H-12), 3.97 (d, *J* =6.1 Hz, 1H, H-6), 5.39 and 5.41 (each br s, 1H, 2 and 9-OH), 6.42 (s, 1H, H-4), 6.51 (s, 1H, H-10), 6.58 (s, 1H, H-7), 6.67 (s, 1H, H-1); FABMS *m/z* 328.234 $[M+H]^+$

*(−)-13aα-Antofine***.** $[\alpha]^{27}_{D}$ −121.1 (*c* 0.05, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 1.78 (m, 1H, H-13β), 1.92 (m, 1H, H-12α), 2.04 (m, 1H, H-12β), 2.25 (m, 1H, H-13α), 2.45 (q, *J* =8.7 Hz, 1H, H-11α), 2.50 (m, 1H, H-13a), 2.90 (dd, *J* =15.6, 10.6 Hz, 1H, H-14β), 3.36 (dd, *J* =15.6, 2.5 Hz, 1H, H-14α), 3.47 (dt, *J* =8.7, 1.7Hz, 1H, H-11β), 3.71 (d, *J* =14.6 Hz, 1H, H-9α), 4.02 (s, 3H, 6-OMe), 4.07 (s, 3H, 2-OMe), 4.11 (s, 3H, 3-OMe), 4.70 (d, *J* =14.6 Hz, 1H, H-9β), 7.21 (dd, *J* =9.1, 2.7 Hz, 1H, H-7), 7.33 (s, 1H, H-1), 7.83 (d, *J* =9.1 Hz, 1H, H-8), 7.91 (d, *J* =2.7 Hz, 1H, H-5), 7.92 (s, 1H, H-4); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ21.8 (C-12), 31.5 (C-13), 34.0 (C-14), 54.1 (C-9), 55.3 (6-OMe), 55.7 (C-11), 56.0 (2-OMe), 56.2 (3-OMe), 60.4 (C-13a), 104.0 (C-4), 104.1 (C-1), 104.8 (C-5), 115.0 (C-7), 123.7 (C-4a), 124.3 (C-8a), 124.4 (C-8), 125.7 (C-14a), 126.9 (C-8b), 127.3 (C-14b), 130.3 (C-4b), 148.5 (C-3), 149.5 (C-2), 157.6 (C-6); FABMS *m/z* 364.223 $[M+H]^+$

*(−)-N-demethylphyllocaryptine***.** $[\alpha]^{27}_{D}$ −80.5 (*c* 0.06, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 2.46 (s, 3H, N-CH_3), 2.55 (dt, *J* =16.1, 5.0 Hz, 1H, H-4eq), 2.70-3.00 (m, 3H, H-3eq, H-α, H-4ax), 3.01 (dd, *J* =14.3, 6.3 Hz, 1H, H-α), 3.15 (ddd, *J* =14.0, 9.0, 5.0 Hz, 1H, H-3ax), 3.66 (t, *J* =6.3 Hz, 1H, H-1), 3.87 (s, 3H, 4'-OMe), 5.54 (brs, 1H, 3'-OH), 5.85 (d, *J* =1.5 Hz, 1H, 6,7-OCH_2O-), 5.88 (d, *J* =1.5 Hz, 1H, 6,7-OCH_2O-), 6.27 (s, 1H, H-8), 6.53 (s, 1H, H-5), 6.59 (dd, *J* =8.0, 2.1 Hz, 1H, H-6'), 6.74 (d, *J* =8.0 Hz, 1H, H-5'), 6.77 (d, *J* =2.1 Hz, 1H, H-2'); ^{13}C-NMR ($CDCl_3$, 150 MHz) δ25.8 (C-4), 41.2 (C-α), 42.8 (N-CH_3), 46.8 (C-3), 56.1 (4'-OMe), 65.3 (C-1), 100.6 (6,7-OCH_2O-), 108.0 (C-8), 108.5 (C-5), 110.5 (C-5'), 115.7 (C-2'), 121.1 (C-6'), 127.4 (C-4a), 131.1 (C-8a), 133.5 (C-1'), 145.0 (C-4'), 145.4 (C-3'), 145.4 (C-7), 146.0 (C-6); FABMS *m/z* 328.221$[M+H]^+$

*(+)-Cinnamolaurine***.** $[\alpha]^{25}_{D}$ +78.9 (*c* 0.50, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 2.47 (s, 3H, N-CH_3), 2.52 (dt, *J* =16.4, 5.0 Hz, 1H, H-4eq), 2.69-2.81 (m, 3H, H-3eq, H-α, H-4ax), 3.02 (dd, *J* =14.3, 5.7 Hz, 1H, H-α), 3.14 (ddd, *J* =14.1, 8.5, 5.0 Hz, 1H, H-3ax), 3.64-3.68 (overlap, H-1), 5.85 (d, *J* =1.5 Hz, 1H, 6, 7-

OCH_2O-), 5.88 (d, *J* =1.5 Hz, 1H, 6, 7-OCH_2O-), 6.23 (s, 1H, H-8), 6.53 (s, 1H, H-5), 6.72 (d, *J* =8.6 Hz, 2H, H-2', 6'), 6.98 (d, *J* =8.6 Hz, 2H, H-3', 5'); FABMS *m/z* 298.207 $[M+H]^+$

*(+)-N-demethylcoculaurine***.** $[\alpha]^{23}_D$ +18.7 (*c* 0.05, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 2.45 (s, 3H, N-CH_3), 2.53 (dt, *J* = 15.1, 4.5 Hz, 1H, H-4_{eq}), 2.69-2.85 (m, 3H, H-3_{eq}, H-α, H-4_{ax}), 3.00 (dd, *J* = 14.3, 6.0 Hz, 1H, H-α), 3.14 (ddd, *J* = 12.5, 8.3, 4.5 Hz, 1H, H-3_{ax}), 3.64-3.68 (overlap, 1H, H-1), 3.85 (s, 3H, 6-OMe), 5.30-5.47 (brs, 2H, 7-, 4'-OH), 6.42 (s, 1H, H-8), 6.52 (s, 1H, H-5), 6.71 (d, *J* = 8.4 Hz, 2H, H-2', 6'), 6.99 (d, *J* = 8.4 Hz, 2H, H-3', 5'); FABMS *m/z* 300.200 $[M+H]^+$

*(−)-Reticuline***.** $[\alpha]^{25}_D$ −60.8 (*c* 0.04, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 2.48 (s, 3H, N-CH_3), 2.56 (dt, *J* = 16.1, 5.0 Hz, 1H, H-4_{eq}), 2.70-2.81 (m, 3H, H-3_{eq}, H-α, H-4_{ax}), 3.00 (dd, *J* = 14.3, 5.6 Hz, 1H, H-α), 3.16 (ddd, J = 14.9, 8.6, 5.0 Hz, 1H, H-3_{ax}), 3.66 (t, *J* = 5.6 Hz, 1H, H-1), 3.85 (s, 3H, 6-OMe), 3.86 (s, 3H, 4'-OMe), 5.38 (s, 1H, 3'-OH or 5-OH), 5.53 (s, 1H, 3'-OH or 5-OH), 6.43 (s, 1H, H-8), 6.54 (s, 1H, H-5), 6.60 (dd, *J* = 8.1, 2.0 Hz, 1H, H-6'), 6.74 (d, *J* = 8.1 Hz, 1H, H-5'), 6.78 (d, *J* = 2.0 Hz, 1H, H-2'); FABMS *m/z* 330.217 $[M+H]^+$