Tirucallane-Type Alkaloids from the Bark of *Dysoxylum laxiracemosum*

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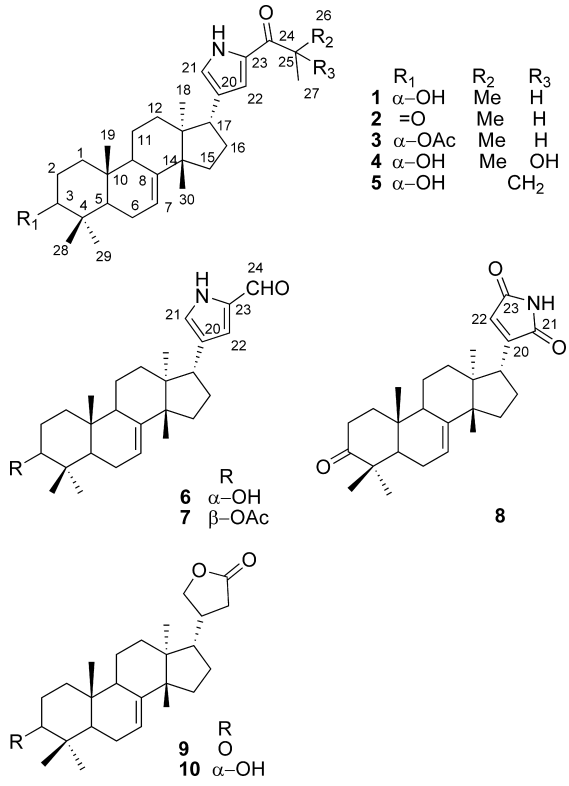
Eight novel tirucallane-type alkaloids (**1**−**8**) and 11 known compounds were isolated from a methanol extract of the bark of *Dysoxylum laxiracemosum*. The structures of **1**−**8** were elucidated using extensive NMR spectrometric and mass spectroscopic methods. Compounds **1** and **5**, named laxiracemosins A and E, showed significant cytotoxicity against five human cancer cell lines.

Plants of the Meliaceae family are rich sources of structurally diverse and biologically significant limonoids.[1] Limonoids are of interest due to their insect antifeedant, growth regulating, antibacterial, antifungal, antimalarial, anticancer, and antiviral activities.[2−4] The chemical constituents of *Dysoxylum laxiracemosum* C. Y. Wu et H. Li (Meliaceae) have not been investigated previously. The present study on the chemical constituents of this species has yielded eight novel tirucallane derivatives (**1**−**8**) with a pyrrole substituent in the side chain. Compounds **6**−**8** were nortirucallane derivatives. To our knowledge, this is the first isolation of tirucallane-type alkaloids. Eleven known compounds were also isolated. The isolation, structural elucidation, and cytotoxicity of compounds **1**−**10** are reported in this paper. Compounds **1**−**10** were evaluated for their cytotoxicity against five human tumor cell lines.



Results and Discussion

The MeOH extract of *D. laxiracemosum* bark was partitioned between EtOAc and H_2O to afford an EtOAc extract, which was subjected to silica gel column chromatography (CC). Fractionation of the extract by repeated CC yielded eight new compounds (**1**−**8**), which were named laxiracemosins A−H.

The molecular formula of laxiracemosin A (**1**) was determined to be $C_{30}H_{45}NO_2$ on the basis of its HRESIMS, requiring nine degrees of unsaturation. The IR spectrum of **1** exhibited absorption bands for −OH, C=O, and C=C groups. Its UV spectrum showed the existence of conjugated groups based on the maximum absorption at 303 nm. The ^{1}H NMR spectrum (Table 1) showed signals of an amine proton (δ_H 10.60), seven methyl groups, and three olefinic protons. Analysis of ^{13}C NMR (Table 3) and HSQC spectra revealed 30 carbon resonances due to one carbonyl, six olefinic, seven methyl, seven methylene, five methine, and four quaternary carbons, accounting for four double-bond equivalents. The remaining five degrees of unsaturation revealed that **1** possessed a pentacyclic skeleton. These data were characteristic of a tirucallane-7-ene system with the exception of the side chain attached to C−17.[5,6] HMBC correlations from δ_H 6.95 (H-21) to δ_C 127.0 (C-20) and 116.1 (C-22) and from δ_H 6.86 (H-22) to δ_C 131.4 (C-23) and 46.2 (C-17) suggested a substituent pyrrole ring at C-17. Furthermore, HMBC correlations from δ_H 1.10 (6H, H-26/27) to δ_C 35.8 (C-25) and 194.2 (C-24) indicated an isopropyl group attached to C-24. A broad singlet for H-3 suggested the β-orientation of H-3.[5,6]

Laxiracemosin B (**2**) possessed the molecular formula $C_{30}H_{43}NO_2$ on the basis of its HRESIMS. Analysis of the ^{1}H and ^{13}C NMR data of **2** (Tables 1 and 3) showed that it had close structural resemblance to **1**, with the exception of a carbonyl (δ_C 216.7) in **2** instead of the methine carbon (δ_C 75.7, C-3) in **1**. The HMBC correlations from δ_H 1.11 (3H, H-30) and 1.03 (3H, H-29) to δ_C 216.7 (C-3) further supported that **2** was the 3-oxo derivative of **1**.

The molecular formula of laxiracemosin C (**3**) was assigned as $C_{32}H_{47}NO_3$ (by HRESIMS). The ^{1}H and ^{13}C NMR data of **3** (Tables 1 and 3) were similar to those of **1**, except for an additional acetyl group [δ_C 170.4 (s), 21.0 (q)]. HMBC correlations from δ_H 1.99 (3H, C$\underline{H}_3$COO) to δ_C 170.4 and 78.4 (C-3) indicated that **3** was the acetate of **1**.

The molecular formula of laxiracemosin D (**4**) was determined to be $C_{30}H_{45}NO_3$ (by HRESIMS). Comparison of the NMR data of **4** (Tables 1 and 3) with those of **1** showed that they were almost identical. The difference was an additional −OH in **4** at C-25, on the basis of the presence of two singlet methyl signals at δ_H 1.45 (6H, H-26/27). The C-25 OH was supported by HMBC correlations from δ_H 1.45 (6H, H-26/27) to δ_C 76.4 (C-25).

The ^{1}H and ^{13}C NMR data of laxiracemosin E (**5**) (Tables 2 and 3) were similar to those of compound **1** except that a methyl (δ_C

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Table 1. ^{1}H NMR Spectroscopic Data of **1**−**4** (δ in ppm and J in Hz)

position	**1**[b]	**2**[a]	**3**[b]	**4**[b]
1a	1.62, m	1.48, m	1.48, m	1.62, m
1b	1.87, m	2.00, m	1.91, m	1.87, m
2a	1.59, m	1.63, m	1.94, m	1.52, m
2b	1.89, m	1.71, m	2.08, m	1.72, m
3	3.37, br s		4.62, br s	3.38, br s
5	1.87, m	1.75, m	1.78, m	1.85, m
6a	1.98, m	2.10, m	1.63, m	1.98, m
6b	2.05, m		1.93, m	2.05, m
7	5.30, br m	5.34, br m	5.31, br m	5.30, br m
9	2.37, m	2.30, m	2.36, m	2.37, m
11	1.61, m	1.61, m	1.61, m	1.61, m
12a	1.30, m	1.45, m	1.25, m	1.29, m
12b	1.46, m	1.85, m	1.42, m	1.45, m
15a	1.60, m	2.21, m	1.61, m	1.75, m
15b	1.74, m	2.73, dd (5.5, 14.5)	1.78, m	1.64, m
16a	1.95, m	1.83, m	1.93, m	1.91, m
16b	2.13, m	2.10, m	2.10, m	2.08, m
17	3.05, dd (9.4, 9.4)	3.02, dd (9.4, 9.4)	3.06, dd (9.3, 9.3)	3.05, dd (9.4, 9.4)
18	0.69, s	0.65, s	0.70, s	0.69, s
19	0.81, s	1.02, s	0.82, s	0.81, s
21	6.95, s	6.82, s	6.95, s	7.05, s
22	6.86, s	6.75, s	6.86, s	6.96, s
25	3.30, m	3.25, m	3.30, m	
26	1.10, br s	1.19, br s	1.10, br s	1.45, s
27	1.10, br s	1.19, br s	1.10, br s	1.45, s
28	0.90, s	1.11, s	0.84, s	0.90, s
29	0.90, s	1.03, s	0.99, s	0.90, s
30	1.11, s	1.11, s	1.10, s	1.10, s
*Me*CO			1.99, s	
N*H*	10.60, br s	9.43, br s	10.58, br s	10.72, br s

[a] Recorded at 400 MHz, in $CDCl_3$. [b] Recorded at 500 MHz, in acetone-d_6.

Table 2. ^{1}H NMR Spectroscopic Data of **5**−**8** (δ in ppm and J in Hz)

position	**5**[a]	**6**[a]	**7**[a]	**8**[b]
1a	1.63, m	1.63, m	1.21, m	1.47, m
1b	1.91, m	1.93, m	1.69, m	2.01, m
2a	1.56, m	1.58, m	1.59, m	2.31, m
2b	1.91, m	1.91, m	1.64, m	2.77, m
3	3.38, br s	3.30, br s	4.46, dd (5.6, 9.0)	
5	1.84, m	1.87, m	1.61, m	1.79, m
6a	1.99, m	2.09, m	2.11, m	2.14, m
6b	2.07, m	2.03, m	2.02, m	
7	5.31, br m	5.31, dd (2.9, 6.7)	5.31, br m	5.35, br m
9	2.37, m	2.37, m	2.34, m	2.29, m
11	1.61, m	1.61, m	1.62, m	1.67, m
12a	1.31, m	1.30, m	1.47, m	1.36, m
12b	1.43, m	1.45, m	1.92, m	2.01, m
15a	1.74, m	1.64, m	1.65, m	1.84, m
15b	1.63, m	1.75, m	1.75, m	1.75, m
16a	1.95, m	1.65, m	1.93, m	1.85, m
16b	2.10, m	1.75, m	2.08, m	2.06, m
17	3.05, dd (9.4, 9.4)	3.15, m	3.06, dd (9.4, 9.4)	3.06, dd (11, 11)
18	0.70, s	0.69, s	0.68, s	0.75, s
19	0.81, s	0.81, s	0.81, s	1.02, s
21	7.02, s	7.07, s	7.06, s	
22	6.71, s	6.86, dd (1.9, 1.9)	6.86, s	6.32, s
24		9.46, d (0.7)	9.45, s	
26a	5.63, s			
26b	5.73, s			
27	1.95, s			
28	0.90, s	0.90, s	0.94, s	1.11, s
29	0.90, s	0.90, s	0.83, s	1.04, s
30	1.10, s	1.10, s	1.10, s	1.12, s
*Me*CO			1.98, s	
N*H*	10.68, br s	10.90, br s	10.90, br s	7.39, br s

[a] Recorded at 400 MHz, in acetone-d_6. [b] Recorded at 500 MHz, in $CDCl_3$.

19.9) and a methine (δ_C 35.8, C-25) in **1** were replaced by a terminal double bond [δ_C 121.8 (t), 145.0 (s)] in **5**. Together with its molecular formula $C_{30}H_{43}NO_2$ based on its HRESIMS, compound **5** was assumed to be a dehydro derivative of **1**. The assumption was supported by HMBC correlations from δ_H 5.63 (1H, H-26) and 5.73 (1H, H-26) to δ_C 145.0 (C-25) and 186.1 (C-24).

The molecular formula of laxiracemosin F (**6**) was $C_{27}H_{39}NO_2$ (by HRESIMS), corresponding to nine degrees of unsaturation. IR absorptions revealed the presence of C═C and −OH groups. The UV spectrum indicated a conjugated system based on the absorption maximum at 303 nm. The ^{1}H NMR spectrum (Table 2) showed signals characteristic of five methyl groups, an amine proton (δ_H

Table 3. ^{13}C NMR Spectroscopic Data for **1**−**8** (**1** and **3**−**7** in acetone-d_6, **2** and **8** in $CDCl_3$, δ in ppm)

position	**1**[a]	**2**[b]	**3**[a]	**4**[b]	**5**[a]	**6**[b]	**7**[b]	**8**[a]
1	31.7, CH_2	38.4, CH_2	31.6, CH_2	31.8, CH_2	31.7, CH_2	32.0, CH_2	37.3, CH_2	38.3, CH_2
2	26.4, CH_2	34.3, CH_2	24.3, CH_2	26.5, CH_2	26.4, CH_2	26.5, CH_2	24.6, CH_2	34.8, CH_2
3	75.7, CH	216.7, qC	78.4, CH	75.7, CH	75.7, CH	75.8, CH	81.1, CH	216.7, qC
4	38.0, qC	47.8, qC	37.2, qC	38.1, qC	38.0, qC	38.1, qC	38.4, qC	47.8, qC
5	45.2, CH	52.3, CH	46.5, CH	45.3, CH	45.2, CH	45.3, CH	51.5, CH	52.3, CH
6	24.6, CH_2	24.3, CH_2	23.5, CH_2	24.7, CH_2	24.5, CH_2	24.6, CH_2	24.4, CH_2	24.3, CH_2
7	118.9, CH	117.9, CH	118.6, CH	118.9, CH	118.9, CH	119.0, CH	118.5, CH	118.8, CH
8	146.8, qC	145.7, qC	146.3, qC	146.9, qC	146.8, qC	146.9, qC	146.6, qC	144.8, qC
9	49.5, CH	48.4, CH	49.5, CH	49.6, CH	49.5, CH	49.7, CH	49.5, CH	48.2, CH
10	35.0, qC	35.1, qC	35.5, qC	35.6, qC	35.5, qC	35.5, qC	35.6, qC	35.1, qC
11	17.9, CH_2	17.5, CH_2	17.9, CH_2	18.0, CH_2	17.9, CH_2	18.0, CH_2	18.0, CH_2	17.4, CH_2
12	31.9, CH_2	30.8, CH_2	32.6, CH_2	32.0, CH_2	31.9, CH_2	31.7, CH_2	31.5, CH_2	30.5, CH_2
13	45.2, qC	44.8, qC	45.1, qC	45.3, qC	45.2, qC	48.2, qC	45.2, qC	46.1, qC
14	51.1, qC	50.4, qC	51.1, qC	51.2, qC	51.2, qC	51.2, qC	51.1, qC	51.5, qC
15	35.8, CH_2	34.8, CH_2	34.9, CH_2	35.1, CH_2	35.0, CH_2	35.0, CH_2	34.9, CH_2	34.2, CH_2
16	27.4, CH_2	26.9, CH_2	27.4, CH_2	27.5, CH_2	27.4, CH_2	27.5, CH_2	27.4, CH_2	26.4, CH_2
17	46.2, CH	45.5, CH	46.2, CH_2	46.2, CH	46.1, CH	46.1, CH	46.0, CH	43.8, CH
18	23.2, CH_3	22.7, CH_3	23.2, CH_3	23.3, CH_3	23.3, CH_3	23.3, CH_3	23.2, CH_3	23.5, CH_3
19	13.4, CH_3	12.7, CH_3	13.2, CH_3	13.4, CH_3	13.4, CH_3	13.4, CH_3	13.4, CH_3	12.7, CH_3
20	127.0, qC	127.0, qC	127.0, qC	127.3, qC	127.2, qC	127.9, qC	127.9, qC	152.5, qC
21	123.7, CH	122.6, CH	123.7, CH	123.7, CH	124.5, CH	125.3, CH	125.3, CH	171.5, qC
22	116.1, CH	115.4, CH	116.1, CH	118.7, CH	118.4, CH	120.6, CH	120.6, CH	128.2, CH
23	131.4, qC	130.5, qC	131.4, qC	128.7, qC	131.0, qC	133.8, qC	133.8, qC	170.5, qC
24	194.2, qC	194.8, qC	194.2, qC	194.1, qC	186.1, qC	179.1, CH	179.1, CH	
25	35.8, CH	35.5, CH	35.8, CH	76.4, qC	145.0, qC			
26	19.9, CH_3	19.6, CH_3	19.9, CH_3	28.5, CH_3	121.8, CH_2			
27	19.9, CH_3	19.6, CH_3	19.9, CH_3	28.5, CH_3	19.0, CH_3			
28	22.2, CH_3	21.5, CH_3	21.6, CH_3	22.2, CH_3	22.2, CH_3	22.2, CH_3	16.1, CH_3	21.5, CH_3
29	28.5, CH_3	24.5, CH_3	27.5, CH_3	27.9, CH_3	28.5, CH_3	28.5, CH_3	27.8, CH_3	24.5, CH_3
30	27.2, CH_3	27.5, CH_3	27.8, CH_3	27.5, CH_3	27.8, CH_3	27.8, CH_3	27.8, CH_3	27.5, CH_3
*Me*CO			21.0, CH_3				21.0, CH_3	
Me*C*O			170.4, qC				170.7, qC	

[a] Recorded at 100 MHz. [b] Recorded at 125 MHz.

10.90), an aldehyde (δ_H 9.46), and three olefinic protons. A combined analysis of ^{13}C NMR (Table 3) and HSQC spectra revealed 27 carbon signals attributed to one aldehyde (δ_C 179.1), six olefinic, five methyl, seven methylene, four methine, and four quaternary carbons. These data suggested that **6** was a degraded derivative of **1**. HMBC correlations from δ_H 9.46 (H-24) to δ_C 133.8 (C-23) and from δ_H 6.86 (H-22) to δ_C 133.8 (C-23) and 179.1 (C-24) revealed that the side chain of **6** was a substituent pyrrole ring conjugated with an aldehyde[7] and that the structure of **6** was as indicated.

Laxiracemosin G (**7**) had the molecular formula $C_{29}H_{41}NO_3$. Comparison of the ^1H and ^{13}C NMR data of **7** (Tables 2 and 3) with those of **6** indicated that **7** was the C-3 acetate of **6**, which was supported by HMBC correlations from δ_H 1.98 (3H, $C\underline{H}_3COO$) to δ_C 170.7 and 81.1 (C-3). Unlike compounds **1** and **3**−**6**, the coupling constants of H-3 in **7** were 5.6 and 9.0 Hz, which suggested the α-orientation for H-3.

The UV spectrum of laxiracemosin H (**8**) showed maximum absorption at 224 nm, which indicated a conjugated group different from that in compounds **1**−**7**. The IR spectrum exhibited absorption bands for NH, C═O, and C═C groups. Similar to compounds **1**−**7**, the ^1H and ^{13}C NMR data (Tables 2 and 3) of **8** showed the tirucallan-7-ene pattern in rings A−D.[6] In combination with the molecular formula $C_{26}H_{35}NO_3$, based on its HRESIMS, the chemical shifts of the remaining four carbons [δ_C 152.5 (s), 128.2 (d), 170.5(s), and 171.5(s)] and NH suggested the presence of a maleimide ring.[8] HMBC correlations from δ_H 6.32 (H-22) to δ_C 170.5 (C-23), 152.5 (C-20), and 43.8 (C-17) and from δ_H 3.06 (H-17) to δ_C 152.5 (C-20) and 171.5 (C-21) confirmed the structure as indicated.

The structures of the known compounds, 3-oxo-24,25,26,27-tetranortirucall-7-ene-23(21)-lactone (**9**),[9] 3-hydroxy-24,25,26,27-tetranortirucall-7-ene-23(21)-lactone (**10**),[9] β-amyrone,[10] β-amyrin,[11] 24,25-epoxytirucall-7-ene-3,23-dione,[12] syringaresinol,[13] scopoletin,[14] 3α-hydroxy-12-ursen-28-oic acid,[15] xylobuxin,[16] piscidinol B,[17] and β-amyrin acetate,[18] were determined by comparing their spectroscopic data with reported values.[9−18]

Table 4. Cytotoxic Activities of Compounds **1**, **2**, **4**, **5**, and **6**

	IC_{50} (μM)				
compound	HL-60	SMMC-7721	A-549	MCF-7	SW480
1	3.1	9.5	5.4	16.8	7.2
2	12.8	19.0	13.4	>20	>20
4	6.8	>20	>20	>20	>20
5	1.5	2.7	3.7	5.1	3.7
6	15.7	15.6	>20	>20	>20
cisplatin	2.4	11.2	17.6	18.7	14.9

Compounds **1**−**10** were evaluated for their cytotoxicity against the HL-60, SMMC-7721, A-549, MCF-7, and SW480 cell lines by the MTT method,[19] and the results are shown in Table 4. The most potent cytotoxic compound was laxiracemosin E (**5**), while compound **1** also showed significant cytotoxicity against these cell lines. Compounds **2**, **4**, and **6** showed some evidence of cytotoxicity against the HL-60 cell line. Compounds **3**, **7**, **8**, **9**, and **10** were inactive against all five cell lines (IC_{50} > 20 μM).

Experimental Section

General Experimental Procedures. Melting points were obtained on an X-4 micro melting point apparatus. Optical rotations were measured with a Horiba SEPA-300 polarimeter. UV spectra were obtained using a Shimadzu UV-2401A spectrophotometer. IR spectra were obtained using a Tenor 27 spectrophotometer and KBr pellets. 1D and 2D NMR spectra were run on Bruker DRX-500 or AV-400 spectrometers with TMS as the internal standard. Chemical shifts (δ) are expressed in ppm with reference to the solvent signals. Mass spectra were recorded on a VG Autospec-3000 spectrometer or an API QSTAR Pulsar I spectrometer. Column chromatography (CC) was performed on silica gel (200−300 mesh, Qingdao Marine Chemical Ltd., Qingdao, People's Republic of China), RP-18 gel (20−45 μm, Fuji Silysia Chemical Ltd., Japan), and Sephadex LH-20 (Pharmacia Fine Chemical Co., Ltd., Sweden). Fractions were monitored by TLC (GF 254,

Qingdao Haiyang Chemical Co., Ltd. Qingdao), and spots were visualized by heating silica gel plates sprayed with 10% H_2SO_4 in EtOH.

Plant Material. *D. laxiracemosum* plants were collected in Xishuangbanna, Yunnan Province, People's Republic of China, and identified by Mr. Jing-Yun Cui, Xishuangbanna Tropical Plant Garden. A voucher specimen (No. Cui20081117) has been deposited at the Kunming Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation. Air-dried and powdered bark of *D. laxiracemosum* (9.7 kg) was extracted with MeOH at room temperature three times (2 days × 3), and solvent was removed under reduced pressure. The residue was partitioned between H_2O and EtOAc. The EtOAc extract (240 g) was subjected to silica gel (200−300 mesh, 2.5 kg) CC, eluting with a $CHCl_3$−Me_2CO step-gradient (1:0, 50:1, 30:1, 20:1, 10:1, 5:1, 2:1, 1:2), to yield fractions 1−5. Fraction 1 (42.5 g) was chromatographed on silica gel (petroleum ether−Me_2CO, 50:1−1:2), silica gel (petroleum ether−EtOAc, 20:1−1:2), and then silica gel (petroleum ether−EtOAc, 15:1−1:2) to give β-amyrone (105 mg), β-amyrin acetate (90 mg), β-amyrin (105 mg), and 24,25-epoxytirucall-7-ene-3,23-dione (206 mg). Fraction 2 (54 g) was chromatographed on silica gel (petroleum ether−Me_2CO, 30:1−1:2) and then silica gel (petroleum ether−EtOAc, 10:1−1:2) to yield **1** (20 mg), **2** (26 mg), **9** (42 mg), and a mixture (10 g), which was subjected to chromatography over RP-18 (MeOH−H_2O, 50%−95%) followed by Sephadex LH-20 ($CHCl_3$−MeOH, 1:1) to give **10** (24 mg), syringaresinol (20 mg), and **7** (5 mg). Fraction 3 (20 g) was subjected to RP-18 CC (MeOH−H_2O, 40%−95%) to give 10 subfractions, 3.1−3.10. Fraction 3.7 (5 g) was applied to silica gel CC (petroleum ether−Me_2CO, 30:1−1:2), silica gel CC (petroleum ether−EtOAc, 12:1−1:2), and then Sephadex LH-20 (MeOH) to yield **3** (12 mg) and **5** (5 mg). Fraction 3.8 (1 g) was chromatographed on silica gel (petroleum ether−EtOAc, 12:1−1:2) to yield scopoletin (10 mg) and **8** (10 mg). Fraction 3.9 (3 g) was subjected to silica gel CC (petroleum ether−EtOAc, 15:1−1:2) to give 3α-hydroxy-12-ursen-28-oic acid (300 mg). Fraction 4 (21 g) was chromatographed over RP-18 (MeOH−H_2O, 40%−95%) to give subfractions 4.1−4.10. Fraction 4.5 (2 g) was chromatographed on silica gel (petroleum ether−EtOAc, 6:1) followed by silica gel CC (petroleum ether−Me_2CO, 12:1−1:2) and Sephadex LH-20 (MeOH) to give piscidinol B (20 mg) and **4** (5 mg). Fraction 4.6 (1 g) was chromatographed on silica gel (petroleum ether−EtOAc, 16:1−1:2) and then silica gel CC (petroleum ether−EtOAc, 10:1−1:2) to yield xylobuxin (11 mg) and a mixture (8 mg), which was chromatographed on Sephadex LH-20 (MeOH) to give **6** (4 mg).

Laxiracemosin A (1): white powder; mp 219−220 °C; $[\alpha]^{25}_D$ +8.9 (*c* 0.3, Me_2CO); UV (MeOH) λ_{max} (log ε) 303 (3.79), 259 (3.45), 206 (4.23) nm; IR (KBr) ν_{max} 3441, 2963, 2871, 1714, 1632 cm^{-1}; ^1H and ^{13}C NMR (acetone-d_6), Tables 1 and 3; positive ion HRESIMS *m/z* 452.3519 (calcd for $C_{30}H_{45}NO_2$ $[M + H]^+$, 452.3528).

Laxiracemosin B (2): white powder; mp 238−240 °C; $[\alpha]^{25}_D$ −7.2 (*c* 0.2, Me_2CO); UV (MeOH) λ_{max} (log ε) 302 (3.84), 258 (3.45), 206 (3.43), 195 (3.34) nm; IR (KBr) ν_{max} 3384, 2939, 2858, 1709, 1636 cm^{-1}; ^1H and ^{13}C NMR ($CDCl_3$), Tables 1 and 3; positive ion HRESIMS *m/z* 450.3380 (calcd for $C_{30}H_{43}NO_2$ $[M + H]^+$, 450.3372).

Laxiracemosin C (3): white powder; mp 267−268 °C; $[\alpha]^{25}_D$ +1.7 (*c* 0.36, Me_2CO); UV (MeOH) λ_{max} (log ε) 302 (3.93), 257 (3.59), 220 (3.07), 207 (3.29) nm; IR (KBr) ν_{max} 3439, 2927, 1720, 1637 cm^{-1}; ^1H and ^{13}C NMR (acetone-d_6), Tables 1 and 3; positive ion HRESIMS *m/z* 516.3448 (calcd for $C_{32}H_{47}NO_3$ $[M + Na]^+$, 516.3453).

Laxiracemosin D (4): white powder; mp 201−202 °C; $[\alpha]^{25}_D$ +10.1 (*c* 0.4, Me_2CO); UV (MeOH) λ_{max} (log ε) 306 (3.88), 262 (3.47), 220 (3.08), 208 (3.25) nm; IR (KBr) ν_{max} 3425, 2948, 1626 cm^{-1}; ^1H and ^{13}C NMR (acetone-d_6), Tables 1 and 3; positive ion HRESIMS *m/z* 490.3290 (calcd for $C_{30}H_{45}NO_3$ $[M + Na]^+$, 490.3297).

Laxiracemosin E (5): white powder; mp 145−146 °C; $[\alpha]^{25}_D$ +18.6 (*c* 0.32, Me_2CO); UV (MeOH) λ_{max} (log ε) 318 (3.78), 220 (3.51), 208 (3.53) nm; IR (KBr) ν_{max} 3433, 2923, 1633 cm^{-1}; ^1H and ^{13}C NMR (acetone-d_6), Tables 2 and 3; positive ion HRESIMS *m/z* 472.3197 (calcd for $C_{30}H_{43}NO_2$ $[M + Na]^+$, 472.3191).

Laxiracemosin F (6): white powder; mp 218−220 °C; $[\alpha]^{25}_D$ +4.7 (*c* 0.3, Me_2CO); UV (MeOH) λ_{max} (log ε) 303 (3.78), 258 (3.53), 220 (2.79), 208 (2.95) nm; IR (KBr) ν_{max} 3431, 2923, 2870, 1641 cm^{-1}; ^1H and ^{13}C NMR (acetone-d_6), Tables 2 and 3; positive ion HRESIMS *m/z* 432.2871 (calcd for $C_{27}H_{39}NO_2$ $[M + Na]^+$, 432.2878).

Laxiracemosin G (7): white powder; mp 270−272 °C; $[\alpha]^{25}_D$ +17.4 (*c* 0.11, Me_2CO); UV (MeOH) λ_{max} (log ε) 303 (3.91), 258(3.64), 206 (3.53), 193 (3.38) nm; IR (KBr) ν_{max} 3406, 2921, 2850, 1719, 1646 cm^{-1}; ^1H and ^{13}C NMR (acetone-d_6), Tables 2 and 3; positive ion HRESIMS *m/z* 452.3157 (calcd for $C_{29}H_{41}NO_3$ $[M + H]^+$, 452.3164).

Laxiracemosin H (8): white powder; mp 225−226 °C; $[\alpha]^{25}_D$ +35.8 (*c* 0.34, Me_2CO); UV (MeOH) λ_{max} (log ε) 279 (2.72), 224 (3.62), 195 (3.44) nm; IR (KBr) ν_{max} 3433, 2953, 1775, 1718, 1624 cm^{-1}; ^1H and ^{13}C NMR ($CDCl_3$), Tables 2 and 3; positive ion HRESIMS *m/z* 410.2692 (calcd for $C_{26}H_{35}NO_3$ $[M + H]^+$, 410.2695).

Cytotoxicity Assay. The following human cancer cell lines were used: human myeloid leukemia HL-60, hepatocellular carcinoma SMMC-7721, lung cancer A-549, breast cancer MCF-7, and colon cancer SW480. All cells were cultured in RPMI-1640 or DMEM medium (Hyclone, USA), supplemented with 10% fetal bovine serum (Hyclone, USA) in 5% CO_2 at 37 °C. The cytotoxicity assay was performed according to the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) method in 96-well microplates.[19] Briefly, 100 μL of adherent cells were seeded into each well of 96-well cell culture plates and allowed to adhere for 12 h before drug addition, while suspended cells were seeded just before drug addition with initial density of 1×10^5 cells/mL. Each tumor cell line was exposed to the test compound at concentrations of 0.0625, 0.32, 1.6, 8, and 40 μM in triplicates for 48 h, with cisplatin (Sigma, USA) as a positive control. After compound treatment, cell viability was detected and a cell growth curve was graphed. IC_{50} values were calculated by Reed and Muench's method.[20]

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Supporting Information Available: 1D and 2D NMR and HRMS spectra of laxiracemosins A−H (**1**−**8**). These materials are available free of charge via the Internet at http://pubs.acs.org.

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