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Gelegamines A–E: five new oxindole alkaloids from *Gelsemium elegans*

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ABSTRACT

Five new oxindole alkaloids, gelegamines A–E (**1**–**5**), were isolated from the roots of *Gelsemium elegans*. Their structures were extensively elucidated on the basis of spectroscopic analysis. Among them, the epoxy ring (C-19/C-20) of gelegamine A (**1**) was assigned as α-orientation by ROESY experiment and DFT method at B3LYP/6-31g(d) level, and gelegamine B (**2**) is the first humantenine-type alkaloid with 19-(*E*) ethylidene configuration. The absolute configurations of gelegamines A–E (**1**–**5**) were established on biosynthetic consideration coupled with CD experiments.

1. Introduction

Gelsemium elegans (Loganiaceae) is a liane native to Southeast Asia, where it is used in folk medicine for the treatment of pain, spasticity, and skin ulcers.[1] In a previous chemical investigation, a number of indole alkaloids based on six different structural skeletons were reported from *G. elegans*.[2] Some of them showed the interesting pharmacological effects, such as analgesic, anti-inflammatory, and antitumor activities.[3] As a part of our ongoing research into alkaloids of chemical, pharmacological, and clinical significance,[4] we investigated the chemical constituents of *G. elegans*, which led to the isolation of two new humantenine-type alkaloids, gelegamines A–B (**1**–**2**) and three new gelsedine-type alkaloids, gelegamines C–E (**3**–**5**), together with 10 known ones. In this paper, we describe the isolation and structural identification of gelegamines A–E. The possible biogenetic relationships of these compounds are discussed.

2. Results and discussion

2.1. Structural elucidation of gelegamines A–E (1–5)

Investigation of the MeOH extract of the roots of *G. elegans* (11.2 kg) resulted in the isolation of 5 new compounds named gelegamines A–E (**1**–**5**) together with 10 known ones: 19(*Z*)-akuammidine,[5] 19(*Z*)-16-*epi*-voacarpine,[6] N_a-methoxytaberpsychine,[7] humantenirine,[8] 11-methoxygelsemamide,[9] gelsenicine,[10] 14-hydroxygelsenicine,[11] 19-oxo-gelsenicine,[2b] koumine,[12] and gelsevirine[13] by comparison of their spectral data with those reported in the literature.

The molecular formula of compound **1** was established as $C_{21}H_{24}N_2O_5$ with HRMS (*m*/*z* 385.1770) $[M+H]^+$. The UV absorption at 218 and 266 nm showed the characteristics of an oxindole nucleus.[2b,8] The ^{1}H NMR spectrum indicated the presence of three aromatic protons attributed to ring A of the oxindole system (δ 7.36, d, *J*=8.5 Hz; 6.59, dd, *J*=8.5, 2.5 Hz; 6.50, d, *J*=2.5 Hz), an N_a-*O*-methyl group at δ 3.94 (3H, s), an *O*-methyl group on the aromatic ring at δ 3.81 (s), an oxymethine proton at δ 3.69 (d, *J*=7.0 Hz, H-3), and oxymethylene protons (H_2-17) at δ 4.36 (m) and δ 4.05 (dd, *J*=10.5, 3.5 Hz) (Table 1).

Twenty-one carbon resonances were also resolved in the ^{13}C NMR spectrum (Table 2), and were further classified via DEPT experiments into 1 carbonyl, 5 quaternary carbons, 9 methines, 3

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Table 1
^{1}H (500 MHz, *J* in Hz) NMR data for compounds **1**–**5**

Position	**1**[a]	**2**[a]	**3**[b]	**4**[a]	**5**[a]
3	3.69 (d, 7.0)	3.75 (d, 6.5)	3.56 (d, 6.0)	3.71 (m)	3.73 (m)
5	4.37 (m)	4.07 (br s)	4.26 (m)	4.42 (m)	4.72 (m)
6	2.54 (dd, 15.5, 7.5), 2.23 (m)	2.24 (dd, 15.5, 5.5), 2.14 (dd, 15.5, 3.0)	2.61 (dd, 15.6, 4.6), 2.52 (dd, 15.6, 2.4)	2.27 (m), 2.35 (m)	2.52 (m), 2.31 (m)
9	7.36 (d, 8.5)	7.26 (d, 8.5)	7.48 (d, 7.5)	7.41 (d, 10.0)	7.42 (d, 10.0)
10	6.59 (dd, 8.5, 2.5)	6.59 (dd, 8.5, 2.5)	7.20 (t, 7.5)	6.57 (dd, 10.0, 2.5)	6.59 (dd, 10.0, 2.5)
11			7.39 (t, 7.5)		
12	6.50 (d, 2.5)	6.54 (d, 2.5)	7.10 (d, 7.5)	6.47 (d, 2.5)	6.48 (d, 2.5)
14	2.44 (m), 2.27 (m)	2.57 (m), 2.32 (dd, 15.0, 4.0)	3.04 (m), 2.31 (m)	2.35 (m), 2.14 (m)	2.29 (m), 2.21 (m)
15	2.09 (m)	3.19 (br m)	2.78 (d, 9.5)	2.59 (br t, 10.0)	2.60 (br t, 10.0)
16	2.41 (m)	2.49 (br s)	3.02 (m)	2.89 (t, 11.5)	3.43 (t, 11.5)
17	4.36 (m), 4.05 (dd, 10.5, 3.5)	4.25 (d, 11.0), 4.18 (dd, 11.0. 2.5)	4.37 (d, 12.0), 4.18 (dd, 12.0, 3.0)	4.28 (m), 4.27 (m)	4.31 (m), 4.29 (m)
18	1.43 (d, 5.5)	1.87 (d, 7.5)	1.39 (d, 6)	1.30 (t, 9.5)	2.66 (s)
19	3.36 (q, 5.5)	7.11 (q, 7.5)	4.61 (m)	2.74 (m), 2.46 (m)	
21	7.32 (1H, s)		4.03 (m), 3.81 (m)		
N_a-Ome	3.94 (s)	3.94 (s)	4.01 (s)	3.94 (s)	3.93 (s)
Ar–OCH_3	3.81 (s)	3.82 (s)		3.81 (s)	3.82 (s)
N_b-Me			3.07 (s)		

[a] Measured in $CDCl_3$.
[b] Measured in CD_3OD.

methylenes, 1 methyl, and 2 *O*-methyl carbons. A comprehensive analysis of the 1D and 2D NMR (^{1}H–^{1}H COSY, HSQC, and HMBC) spectra indicated that **1** is an analogue of humantenirine.[8] Two oxygenated carbons at δ 59.6 and 58.5 were assigned to C-19 and C-20, respectively, as part of an epoxide, by the HMBC correlations from H-15 and H_3-18 to C-19 and C-20, whereas an imine carbon at δ 162.4 was assigned to C-21 by the HMBC correlations from H-21 to C-15, C-19, and C-20. Therefore, the chemical structure of **1** was established as shown in Figure 1.

The relative configuration of **1** was deduced from ROESY experiments and molecular modeling (Gaussian D.01)[14] using ab initio calculations. In the ROESY spectrum, the cross peaks observed between the proton pairs H-3/H_2-14, H_2-14/H-15, H-9/H-6, H-6/H-5, and H-5/H-16 indicated that the relative configuration of C-3, C-5, C-15, and C-16 in **1**, as shown (Fig. S6, Supplementary data), is identical to that in humantenirine.[8] The ROESY correlation between H-19 and H-21 indicated that both protons were on the same side. Although ROESY correlations of H_3-18/H-14a, H_3-18/H-14b, H_3-18/H-15, and H-19/H-21 were unambiguous, it is not sufficient to determine the orientation of the C-19/C-20 epoxy ring. Therefore, DFT calculations at the B3LYP/6-31G (d) level were made for the two possible structures of **1**, corresponding to the α (**A**) or β (**B**) orientations of the C-19/C-20 epoxy ring as shown in Figure 2. Two optimized structures were obtained, in which the calculated distance of the proton pairs near the epoxide oxygen of **A** was fully consistent with the corresponding ROESY data. Therefore, the orientation of the C-19/C-20 epoxy ring was determined to be α.

Table 2
^{13}C (100 MHz) NMR data for compounds **1**–**5**

Position	**1**[a]	**2**[a]	**3**[b]	**4**[a]	**5**[a]
2	172.4	172.6	177.2	171.7	171.6
3	73.5	73.5	76.2	75.2	75.5
5	59.2	53.5	72.4	72.0	74.4
6	35.9	38.0	29.8	37.8	38.2
7	55.6	55.0	58.2	55.4	55.9
8	123.2	121.3	131.5	123.9	123.6
9	125.3	125.7	126.7	125.4	125.3
10	107.8	107.8	125.3	107.7	107.9
11	160.2	160.4	130.2	160.1	160.3
12	94.3	94.7	109.2	93.9	94.0
13	139.2	139.9	139.9	139.1	139.1
14	25.1	29.8	24.0	26.9	27.4
15	28.0	27.5	38.0	39.6	39.3
16	31.3	34.8	37.5	42.5	38.9
17	66.4	65.9	63.4	62.0	61.7
18	14.4	14.2	20.5	9.9	26.1
19	59.6	136.9	65.6	25.6	197.6
20	58.9	133.4	78.7	185.1	178.0
21	162.4	166.5	62.4		
N_a-OMe	63.4	63.6	64.5	63.4	63.4
Ar–OCH_3	55.6	55.6		55.5	55.6
N_b-Me			35.0		

[a] Measured in $CDCl_3$.
[b] Measured in CD_3OD.

The molecular formula of compound **2** was established as $C_{21}H_{24}N_2O_5$ with HRMS (*m*/*z* 385.1756) $[M+H]^+$, UV absorption revealed an oxindole nucleus.[2b,8] The ^{13}C NMR (Table 2) and DEPT spectra showed the presence of 21 carbon signals composed of 2 carbonyl carbons, 8 double-bond carbons (6 aromatic and 2 vinylic), and 11 sp^3 carbons (2 *O*-methyls, 1 methyl, 3 methylenes, 4 methines, and 1 quaternary carbon). The spectroscopic properties of **2** were reminiscent of those of humantenirine.[8] The main difference from humantenirine was a methylene at C-21 in the later was replaced by a conjugated carbonyl carbon (δ_C 166.5) due to UV absorption bond at 256 nm. The HMBC correlations from H-15, H-19 and H_3-18 to C-21 verified this deduction. In addition, by comparison of chemical shift of C-15 in **2** with that of humantenirine, a obvious upfield-shift about 6.8 ppm was observed, this suggested the configuration of C-18 in **2** should be *E*-geometry due to γ-*gauche* effect between C-15 and C-18 in **2**, which was further confirmed by strong ROESY correlation of H-15/H_3-18. Based on further 2D-NMR analysis, the structure of **2**, gelegamine B, was determined as shown

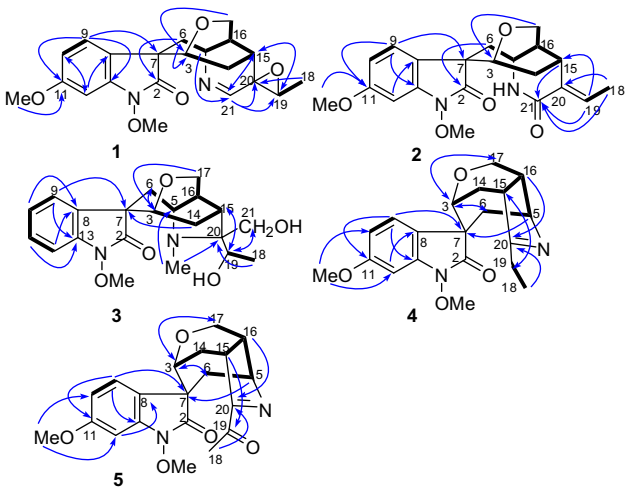
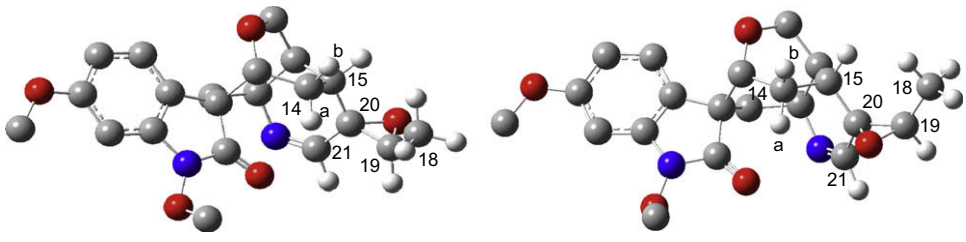


Figure 1. ^{1}H–^{1}H COSY (bold) and HMBC (arrow, H→C) correlations for compounds **1**–**5**.



	(0)	(0.28)
H_3-18/H-14a	2.80Å	4.23Å
H3-18/H-14b	2.74Å	3.66Å
H3-18/H-15	2.34Å	2.10Å
H-19/H-21	2.37Å	2.52Å

Figure 2. Two DFT-optimized possible structures (**A** and **B**) were found for gelegamine A (**1**). Energies in kcal/mol relative to the more stable one (**A**) are given in parentheses. Calculated distance of the proton pairs near the epoxide in the two structures is also available.

(Figs. 1 and 3). To best of our knowledge, compound **2** is the first humantenine-type alkaloid with 19-(*E*) ethylidene configuration.

The molecular formula of the alkaloid **3** was established as $C_{21}H_{28}N_2O_5$ with HRMS (*m*/*z* 389.2077 $[M+H]^+$). The ^1H and ^{13}C NMR data (Tables 1 and 2) showed the presence of 1 carbonyl, 3 double-bonds (2 trisubstituted and 1 disubstituted), and 14 sp^3 carbons (1 N_a-*O*-methyl, 2 methyls, 4 methylenes, 5 methines, and 2 quaternary carbons). Comparison of the NMR data for **3** with those of 19-hydroxy-11-methoxygelselegine,[15] which showed that their chemical shifts were similar, except for the lack of the *O*-methyl signal at C-11 and the presence of a methyl carbon signal at δ 35.0 ppm. The downfield shift of ~10 ppm for C-5 and C-20 in **3** relative to those in 19-hydroxy-11-methoxygelselegine suggests that the methyl group is connected to N_b. All the NMR data imply that gelegamine C (**3**) is 19-hydroxy-N_b-methylgelselegine, which was confirmed with 2D NMR experiments. The planar structure and the relative configuration of **3** are shown in Figures 1 and 3, respectively.

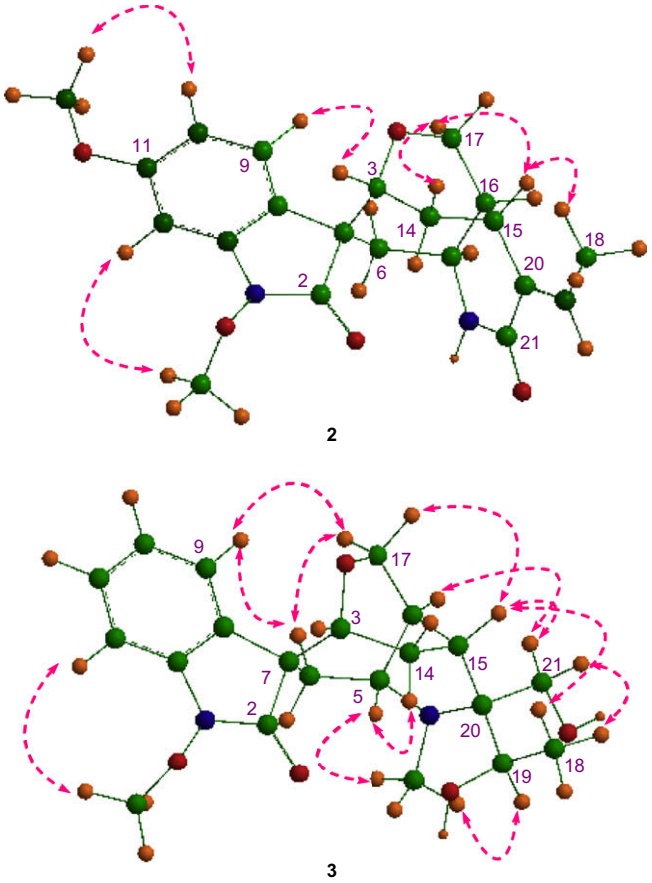


Figure 3. ROESY (dashed) correlations for gelegamines B and C (**2** and **3**).

The HRMS analysis of the new alkaloid **4**, showed a protonated molecular ion peak at *m*/*z* 357.1817 ($[M+H]^+$), corresponding to the molecular formula $C_{20}H_{24}N_2O_4$ (*m*/*z* 356.1736). The UV absorption at 261 (3.55), 240 (3.67), and 217 (3.49) nm revealed the presence of an oxindole nucleus.[2b] The ^1H NMR spectrum of **4** (Tables 1 and 2) exhibited characteristic signals for a 1,2,4-trisubstituted phenyl group (δ 6.47, d, *J*=2.5 Hz; 6.57, dd, *J*=10.0, 2.5 Hz; 7.41, d, *J*=10.0 Hz), an N_a-*O*-methyl group (δ 3.94, s), an *O*-methyl group (δ 3.81, s), an oxymethine group (δ 3.71, m, H-3), an oxymethylene (δ 4.28, m; 4.27, m, H_2-17), and an ethyl group (δ 1.30 [3H, t, *J*=9.5 Hz, H_3-18], 2.74, m, 2.46, m [each 1H, H_2-19]). Comparison of the NMR data of **4** with those of the known alkaloid gelsenicine[10] indicated that their chemical shifts were similar, except for the signals of the aromatic protons, suggesting that compound **4** is a gelsenicine derivative, with an *O*-methyl group attached to either C-10 or C-11. The presence of an HMBC correlation between H-10 (δ 6.57, dd, *J*=10.0, 2.5 Hz) and *O*-methyl carbon (δ 55.5) and a ROESY correlation between H-3 and H-9 unambiguously led to the conclusion that the *O*-methyl group is located at C-11. Thus, the structure of gelegamine D (**4**) was assigned as shown in Figure 1.

The molecular formula of alkaloid **5** was established as $C_{20}H_{22}N_2O_5$ with HRMS (*m*/*z* 393.1420 $[M+Na]^+$). The UV spectrum displayed the characteristics of an oxindole nucleus, and the IR spectrum displayed absorption of a carbonyl group at 1714 cm^{-1}. The ^1H NMR spectrum showed the signals of a methine proton at δ 4.72 (m) connected to the nitrogen atom of an imine functional group, three aromatic protons attributed to ring A of the oxindole system (δ 7.42 [d, *J*=10.0 Hz]; 6.59 [dd, *J*=10.0, 2.5 Hz]; 6.48 [d, *J*=2.5 Hz]), and oxymethylene protons at δ 4.29 (m) and 4.31 (m) (H_2-17) (Table 1). The ^{13}C and DEPT NMR spectra revealed the existence of a conjugated ketone carbonyl carbon at δ 197.6, an imine carbon at δ 178.0, an N_a-*O*-methyl carbon at δ 63.4, a regular *O*-methyl carbon at δ 55.6, a methyl carbon at δ 26.1, a methine carbon at δ 74.4, and a carbonyl carbon at δ 171.6 (Table 2). The ^1H and ^{13}C NMR spectra of **5** are very similar to those of GS-1,[16] except for the lack of a hydroxyl group at C-14. Thus, the structure of **5** was deduced to be 14-deoxy GS-1, namely gelegamine E, which was confirmed by 2D NMR experiments.

The similar patterns of Cotton effects in the CD spectra corresponding to the UV absorption maxima of alkaloids **1**–**4** (Fig. 4) indicate that the chiral centers have an absolute configuration identical to that of other known analogues.[2b,10,17]

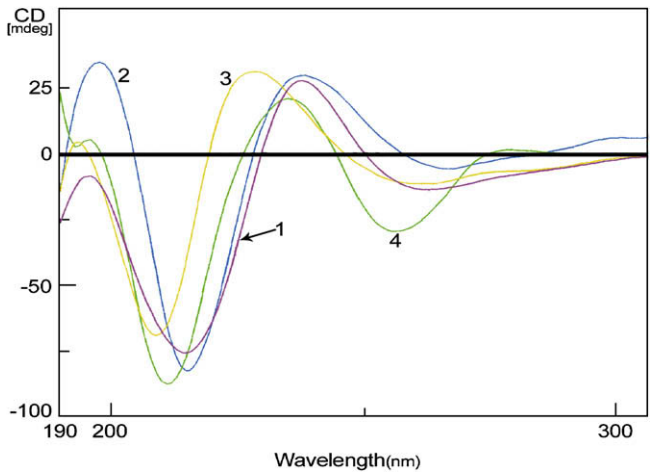


Figure 4. CD spectra for gelegamines A–D (**1**–**4**) (in MeOH).

2.2. Possible biogenetic route for gelegamines A–E (1–5)

With consideration of the new compounds gelegamines A–E (**1**–**5**) isolated from the title plant, a systematic biogenetic pathway from 19-(*E*) ethylidene configuration sarpagine-type alkaloids to gelsedine-type alkaloids was proposed via the sequence as described in Scheme 1: (i) transformation of the sarpagine-type indole alkaloid, gardnerine,[2b] into a C/D ring opening compound, 11-methoxyltaberpsychine;[2b] (ii) oxidation rearrangement and methoxylation of N_a function[17,18a] from 11-methoxyltaberpsychine to 19*E*-humantenine-type intermediate **7**; (iii) epoxidation from **7** to the key intermediate **9**; (iv) semipinacol rearrangement of **9** to form intermediate **11** with a tetrahydropyrrole and aldehyde functionality; (v) oxidative cleavage of C-21 in **11** to form a gelsedine-type alkaloid **12**, which could be further converted to **4** or **5** via reduction and oxidation, respectively.[18]

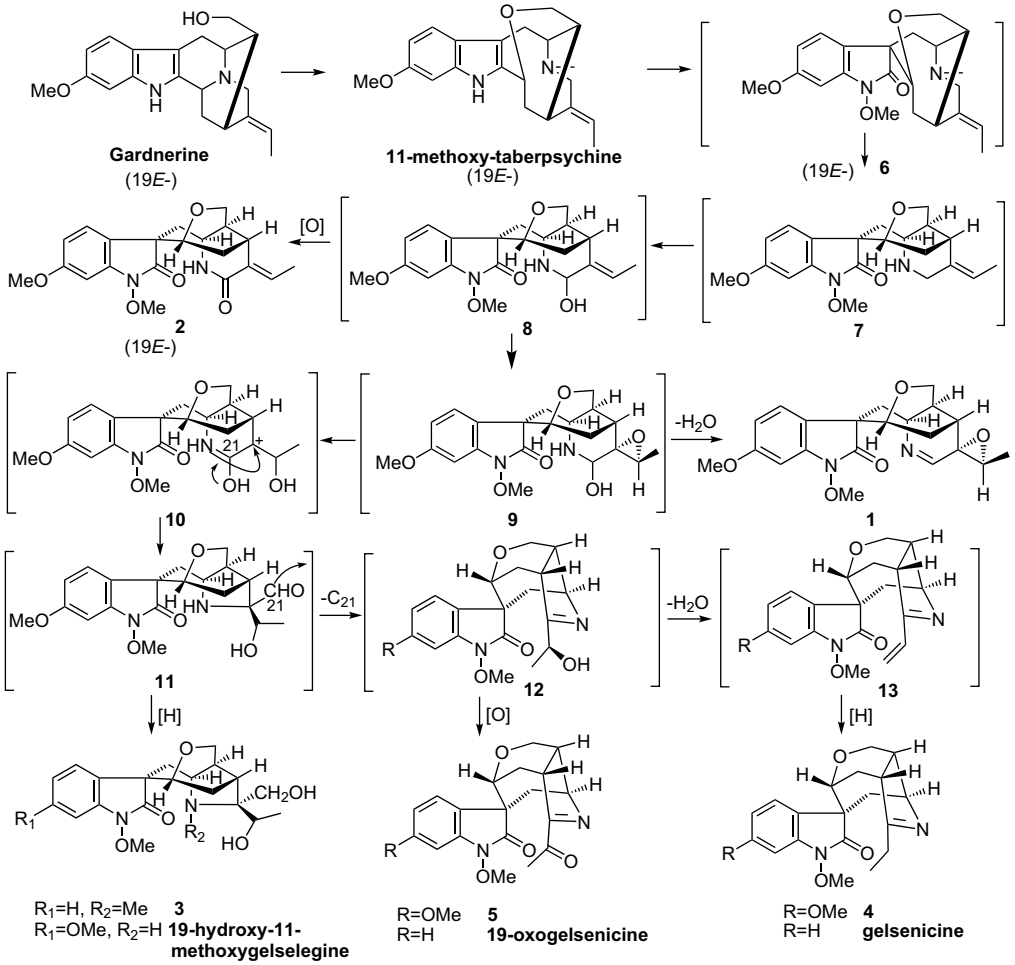
2.3. Activity test

The cytotoxic activity of compounds **3**–**5** and 10 known ones against HL-60 human leukemia and A-549 human lung cancer cell lines were evaluated by follow the standard protocols MTT[19] and SRB[20] methods, respectively. And pseudolaric acid B[21] was used as a positive control. But none showed obvious effects (IC_{50}> 1.0×10^{-5} M).

3. Experimental section

3.1. General

Optical rotations were measured on a Perkin–Elmer 241 polarimeter. UV spectra were obtained on a UV-210A spectrometer. CD spectra were recorded on a JASCO J-810 spectropolarimeter. IR spectra were recorded on a Bio-Rad FTS-135 spectrometer with KBr pellets. NMR spectra were recorded on a Bruker AM-500



Scheme 1. Hypothetical biogenetic pathway for *Gelsemium* alkaloids.

spectrometer with TMS as the internal standard. ESIMS were carried out on a Finnigan MAT 90 mass spectrometer and VG Auto Spec-3000 instrument, respectively. Chromatographic separations were performed on silica gel (90–150 μm; Qingdao Marine Chemical Plant, Qingdao, China) columns, Sephadex LH-20 (40–70 μm; Amersham Pharmacia Biotech AB, Uppsala, Sweden) columns, or Lichroprep RP-18 gel (40–63 μm; Merck, Darmstadt, Germany) columns. Semipreparative HPLC was performed on a Zorbax SB-C18 (10 μm; Agilent Co., Ltd. Wilmington, Delaware) column (i.d. 9.4×250 mm), eluted with CH_3OH–H_2O (50:50; for 30 min at a flow rate of 3.0 mL/min; detection, UV 254 nm, 280 nm) at 30 °C. Precoated silica gel GF_{254} and HF_{254} plates (Qingdao Haiyang Chemical Plant, Qingdao, China) were used for TLC.

3.2. Plant material

The roots of *G. elegans* were collected in Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences, Yunnan Province, China, in April 2006. The plant was identified by Prof. De-Ding Tao and a voucher specimen (KIB 06051011) was deposited in the Herbarium of Kunming Institute of Botany, Chinese Academy of Sciences.

3.3. Extraction and isolation

The air-dried roots of *G. elegans* (11.2 kg) were percolated with MeOH three times at room temperature and twice under reflux. The combined MeOH extracts were concentrated and the residue (135 g) was suspended in 1.5 L of water, acidified with 5% HCl to pH 3, and partitioned with EtOAc to remove the neutral components. The aqueous phase was then adjusted to pH 9 with a saturated solution of Na_2CO_3 before $CHCl_3$ extraction. The combined organic phases were concentrated to yield a crude alkaloid mixture (44.6 g), which was subjected to silica gel open-column chromatography, eluted with a $CHCl_3$–MeOH gradient to yield seven fractions (Fr. A–G). Fraction C (160 mg) was subjected to silica gel column chromatography using a gradient solvent system containing petroleum ether–acetone–Et_2NH (30:1:0.1 to 5:1:0.1) to yield gelsenicine (23 mg), 14-hydroxygelsenicine (7 mg), 19-oxo-gelsenicine (9 mg), and an alkaloid mixture (Fr. C1). The subfraction Fr. C1 was separated on a silica gel column eluted with petroleum ether–acetone–Et_2NH (5:1:0.1 to 3:1:0.1) to yield gelegamine D (**4**, 9 mg), gelegamine E (**5**, 4 mg), 19(*Z*)-akuammidine (3 mg), 19(*Z*)-16-*epi*-voacarpine (7 mg), and another alkaloid mixture, which was further separated by semipreparative HPLC (C_{18} reversed-phase silica gel column, MeOH–H_2O [50:50]) to yield gelegamine C (**3**, 6.8 mg). Fraction D (120 mg) was separated chromatographically on a silica gel column, eluted with petroleum ether–acetone–Et_2NH (15:1:0.1 to 3:1:0.1), to yield six compounds: gelegamine A (**1**, 10 mg), gelegamine B (**2**, 14 mg), gelsevirine (6 mg), humantenirine (7 mg), 11-methoxygelsemamide (8 mg), koumine (11 mg), and N_a-methoxyanhydrovobasinediol (14 mg), in that order.

3.4. Characteristics of alkaloids 1–5

3.4.1. Gelegamine A (**1**)

Amorphous; [α] −373.3 (*c* 0.60, MeOH); UV (MeOH) λ_{max} (log ε) 266 (3.42), 218 (3.23) nm; CD (*c* 1.43 mmol/L, MeOH, 25 °C) Δε (nm) −13.81 (263), +27.49 (238), −75.76 (215), −8.68 (196); IR (KBr) ν_{max} 3426, 2926, 1721, 1628, 1497, 1216, 1109, 1040, 997, 877 cm^{-1}; ^1H and ^{13}C NMR (measured in $CDCl_3$), see Tables 1 and 2; ESI-MS *m*/*z* 385.3 $[M+H]^+$; HRESIMS *m*/*z* 385.1770 (calcd for $C_{21}H_{24}N_2O_5$, 384.1685).

3.4.2. Gelegamine B (**2**)

Amorphous; [α] −186.1 (*c* 0.60, MeOH); UV (MeOH) λ_{max} (log ε) 256 (3.50), 219 (4.47) nm; CD (*c* 38.03 mmol/L, MeOH, 25 °C) Δε (nm) −1.01 (268), +5.80 (238), −15.87 (215), +6.78 (198); IR (KBr) ν_{max} 3433, 2927, 1722, 1628, 1441, 1217, 1078, 966, 772 cm^{-1}; ^1H and ^{13}C NMR (measured in $CDCl_3$), see Tables 1 and 2; ESI-MS *m*/*z* 385.4 $[M+H]^+$; HRESIMS *m*/*z* 384.1756 (calcd for $C_{21}H_{24}N_2O_5$, 384.1763).

3.4.3. Gelegamine C (**3**)

Amorphous; [α] −61.5 (*c* 0.13, MeOH); UV (MeOH) λ_{max} (log ε) 256 (4.05), 208 (4.71) nm; CD (*c* 70.62 mmol/L, MeOH, 25 °C) Δε (nm) −8.71 (262), +23.50 (229), −52.16 (209), +3.38 (194); IR (KBr) ν_{max} 3421, 2925, 1710, 1618, 1464, 1238, 1038, 997, 750 cm^{-1}; ^1H and ^{13}C NMR (measured in CD_3OD), see Tables 1 and 2; ESI-MS *m*/*z* 388 $[M+H]^+$; HRESIMS *m*/*z* 389.2077 $[M+H]^+$ (calcd for $C_{21}H_{28}N_2O_5$, 388.1998).

3.4.4. Gelegamine D (**4**)

Amorphous; [α] −87.0 (*c* 0.09, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 261 (3.55), 240 (3.67), 223 (3.50), 217 (3.49) nm; CD (*c* 1.40 mmol/L, MeOH, 25 °C) Δε (nm) −24.62 (257), +17.72 (236), −73.28 (211), +4.58 (196); IR (KBr) ν_{max} 3436, 2924, 1724, 1598, 1461, 1216, 879, 715 cm^{-1}; ^1H and ^{13}C NMR (measured in $CDCl_3$), see Tables 1 and 2; ESI-MS *m*/*z* 357.0 $[M+H]^+$; HRESIMS *m*/*z* 357.1517 (calcd for $C_{20}H_{24}N_2O_4$, 356.1736).

3.4.5. Gelegamine E (**5**)

Amorphous; [α] −303.3 (*c* 0.05, $CHCl_3$); UV (MeOH) λ_{max} (log ε) 268 (3.89), 240 (4.07), 223 (4.82), 216 (3.82) nm; IR (KBr) ν_{max} 3429, 2923, 1714, 1626, 1496, 1215, 1038, 988, 825 cm^{-1}; ^1H and ^{13}C NMR (measured in $CDCl_3$), see Tables 1 and 2; ESI-MS *m*/*z* 371.3 $[M+H]^+$; HRESIMS *m*/*z* 393.1420 $[M+Na]^+$ (calcd for $C_{20}H_{22}N_2O_5$, 370.1529).

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.03.086.

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