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# Glabcensin V–Y, four *ent*-kaurane diterpenoids from *Isodon angustifolius* var. *Glabrescens*

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**Abstract**

Four new *ent*-kaurane diterpenoids, glabcensin V–Y were isolated from the dried leaves of *Isodon angustifolius* var. *glabrescens* and their structures elucidated by spectral methods. The structures of the new compounds were established as *ent*-6β,11α-dihydroxy-3α,7α-diacetoxy-kaur-16-ene-15-one; *ent*-3α,6β,7α,11α-tetraacetoxy-kaur-16-ene-15-one; *ent*-3α-hydroxy-7α,11α-diacetoxy-kaur-16-ene-6,15-dione and *ent*-3α,15α-dihydroxy-7α,11α-diacetoxy-kaur-16-ene-6-one respectively. 

*Keywords: Isodon angustifolius* var. *glabrescens*; Labiatae; *Ent*-kaurenoids; Glabcensin V–Y

## 1. Introduction

In previous papers (Zhao, Tian, Yue, Lin, & Sun, 1997; Zhao, Jiang, Wang, Lin, & Sun, 1998), we reported on the isolation and structure determination of glabcensin A–U from the dried leaves of *Isodon angustifolius* var. *glabrescens* (Wu & Li, 1979). Further investigation on the constituents of this species led to the isolation of four new diterpenoids, named as glabcensin V–Y. This paper describes the isolation and elucidation of these new diterpenoids.

## 2. Results and discussion

Glabcensin V (**1**), $C_{24}H_{34}O_7$ ($[M]^+ = m/z$ 434), was obtained as an amorphous powder. The $^1H$ and $^{13}C$ NMR spectra resembled those of dowoensin A (**5**) (Zhao et al., 1991; Sun et al., 1995), except for the presence of a hydroxyl group in place of the acetoxyl group at C-6. This conclusion was confirmed as follows. The upfield shift of the H-6β signal from $\delta$ 5.33 (1H, dd, $J = 4,2$ Hz) in dowoensin A to $\delta$ 4.36 (1H, dd, $J = 3.6$, 1.8 Hz, H-6β) in **1** placed the hydroxyl group at the C-6α position. Thus, glabcensin V (**1**) was identified as *ent*-6β,11α-dihydroxy-3α,7α-diacetoxy-kaur-16-ene-15-one.

Glabcensin W (**2**), $C_{28}H_{38}O_9$ ($[M]^+ = m/z$ 518), was obtained as an amorphous powder. It showed similar spectral data to those of dowoensin A (**5**) (Zhao et al., 1991; Sun et al., 1995). The difference between **2** and dowoensin A was that **2** had one more acetoxyl group and one less hydroxyl group than dowoensin A. The downfield shift of the H-11α signal from $\delta$ 4.76 (1H, *t*, $J = 3.5$ Hz) in dowoensin A to $\delta$ 5.30 (1H, t, $J = 4.0$ Hz, H-11α) in **2** placed the acetoxyl group at the C-11β position. Thus, glabcensin W (**2**) was characterized as *ent*-3α,6β,7α,11α-tetraacetoxy-kaur-16-ene-15-one.

Glabcensin X (**3**), $C_{24}H_{32}O_7$ ($[M]^+ = m/z$ 432), was obtained as an amorphous powder. The $^1H$ and $^{13}C$ NMR spectra resembled those of xindongnin A (**6**) (Sun, Lin, Fu, Zheng, & Gao, 1985; Zhao et al., 1991), except for the presence of the hydroxyl group in place of the acetoxyl group at C-3 and the acetoxyl group in place of the hydroxyl at C-11. This conclusion was confirmed as follows. The upfield shift of the H-3α signal from $\delta$ 4.71 (1H, t, $J = 3.0$ Hz) in xindongnin A to $\delta$ 3.82 (1H, t, $J = 3.0$ Hz, H-3α) in **3** placed the hydroxyl group at the C-3α position. The downfield shift of the H-11α signal from $\delta$ 4.32 (1H, t, $J = 4.0$ Hz) in xindongnin A to $\delta$ 5.12 (1H, t, $J = 5.0$ Hz, H-11α) in **3** placed the acetoxyl group at the C-11α

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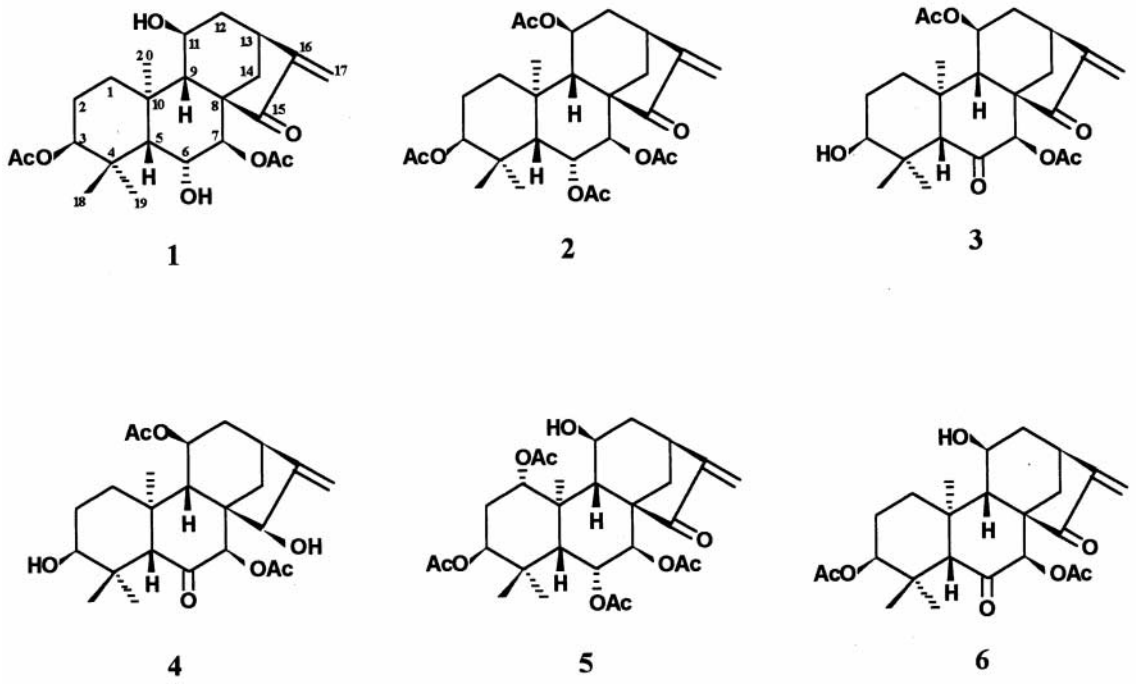


position. Thus, glabcensin X (**3**) was identified as *ent*-3α-hydroxy-7α,11α-diacetoxy-kaur-16-ene-6,15-dione.

Glabcensin Y (**4**), $C_{24}H_{34}O_7$ ($[M]^+ = m/z$ 434), an amorphous powder, showed similar spectral data to those of glabcensin X (**3**). This compound showed no characteristic absorption bands for a ketone conjugated with an *exo*-methylene in its UV (no maximum above $\lambda_{max}$ 220 nm) and IR spectra, but gave rise to the signals of an *exo*-methylene moiety [$\delta$ 5.38, 5.29 (each 1H, br s, $H_2$-17) in its $^1$H NMR $\delta$ 157.86 (s), 107.04 (t)] in its $^{13}$C NMR spectra) and the signal of an isolated ketone ($\delta$ 207.97) in its $^{13}$C NMR spectrum. Its mass spectrum showed a $[M]^+$ ion at $m/z$ 434, i.e. 2 amu more than that of **3**. All the above evidence suggested that glabcensin Y (**4**) should have a structure corresponding to dihydroglabcensin X in which the ketone group at C-15 was reduced to an allylic alcohol. Based on the upfield shift of C-9 ($\delta$ 50.05) due to the γ-steric compression effect between 15β-OH and C-9 (Wu, Zhang, Chen, Lin, & Sun, 1993), the configuration of the hydroxyl group at C-15 was β. Thus, glabcensin Y (**4**) was elucidated as *ent*-3α,15α-dihydroxy-7α,11α-diacetoxy-kaur-16-ene-6-one.

## 3. Experimental section

### 3.1. General

M.p.: uncorr.; UV: MeOH; IR: KBr; EIMS: 70 eV; $^1$H and $^{13}$C NMR: 400 and 100 Hz, with TMS as int. standard. Chemical shift values were reported in $\delta$ (ppm) units, the solvent ($C_5D_5N$) signals as int. ref.

### 3.2. Plant material

Plant material was collected in Dali county, Yunnan province, People's Republic of China, in September 1993, and identified as *I. angustifolius* (Dunn) var. *glabrescens* by Professor X.-W. Li. A voucher specimen (No. 930932-KIB) is deposited in the herbarium of the Department of Taxonomy, Kunming Institute of Botany.

### 3.3. Extraction and isolation

Dried leaves (3.0 kg) of *I. angustifolius* var. *glabrescens* were extracted exhaustively with 95% EtOH (5 l × 3) under reflux. The extract was concd in vacuo to give a residue (300 g) which was chromatographed over silica gel (200–300 mesh, 1.5 kg). The column was eluted with $CHCl_3$–$Me_2CO$ (9.5: 0.95, 9:1, 8:2, 7:3, 6:4) and $Me_2CO$. 500 ml each fractions were collected. All components were purified by CC (including CC on MCI gel CHP-20, RP-18 and RP-8 gel) and HPLC. Recrystallization finally afforded compounds **1** (100 mg), **2** (91 mg), **3** (20 mg) and **4** (50 mg).

### 3.4. Glabcensin V (**1**)

$C_{24}H_{34}O_7$, an amorphous powder, $[\alpha]_D^{22}$: −7.32° ($CHCl_3$, *c* 0.48). UV $\lambda_{max}^{MeOH}$ nm (log ε): 238 (3.77); IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3450, 2905, 1715, 1635, 1465, 1250, 1030; EIMS $m/z$ (rel. int.): 434 $[M]^+$ (2), 374 $[M–AcOH]^+$ (32), 314 $[M–2 \times AcOH]^+$ (50), 299 $[M–2 \times AcOH–Me]^+$ (100), 281 $[M–2 \times AcOH–Me–H_2O]^+$ (45); $^1$H NMR $\delta$: 4.82 (1H, br s, H-3α), 2.59 (1H, br s, H-5β),

Table 1. $^{13}C$ NMR data of compounds **1**–**6** (pyridine-$d_5$)

| C | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| 1 | 36.6 t | 36.2 t | 34.3 t | 34.3 t | 35.5 t | 35.5 t |
| 2 | 23.1 t | 22.8 t | 25.9 t | 26.0 t | 20.7 t | 22.6 t |
| 3 | 79.1 d | 78.2 d | 75.0 d | 74.6 d | 78.3 d | 77.2 d |
| 4 | 37.4 s | 36.8 s | 38.6 s | 37.4 s | 36.9 s | 35.8 s |
| 5 | 44.5 d | 43.7 d | 53.8 d | 50.1 d | 43.5 d | 54.8 d |
| 6 | 69.1 d | 70.0 d | 202.3 s | 208.0 s | 70.3 d | 202.2 s |
| 7 | 76.3 d | 71.3 d | 80.7 d | 84.2 d | 71.4 d | 80.4 d |
| 8 | 49.1 s | 48.6 s | 45.9 s | 51.1 s | 48.4 s | 53.4 s |
| 9 | 59.9 d | 55.8 d | 56.7 d | 54.5 d | 59.2 d | 59.1 d |
| 10 | 38.5 s | 38.6 s | 45.9 s | 43.6 s | 38.2 s | 44.8 s |
| 11 | 65.2 d | 68.1 d | 68.2 d | 68.5 d | 64.7 d | 64.7 d |
| 12 | 41.2 t | 38.3 t | 39.5 t | 40.2 t | 40.8 t | 40.7 t |
| 13 | 37.8 d | 37.1 d | 37.2 d | 37.4 d | 37.4 d | 36.8 d |
| 14 | 35.1 t | 34.3 t | 32.9 t | 36.5 t | 35.6 t | 34.4 t |
| 15 | 207.0 s | 204.6 s | 202.3 s | 80.0 s | 205.1 s | 206.5 s |
| 16 | 151.9 s | 150.4 s | 151.2 s | 157.9 s | 151.2 s | 151.1 s |
| 17 | 110.5 t | 113.0 t | 114.0 t | 107.0 t | 111.1 t | 112.6 t |
| 18 | 28.5 q | 28.1 q | 28.1 q | 28.4 q | 28.0 q | 27.0 q |
| 19 | 24.1 q | 23.4 q | 22.9 q | 22.9 q | 23.2 q | 22.0 q |
| 20 | 19.5 q | 19.3 q | 19.2 q | 18.8 q | 19.2 q | 18.5 q |
| OAc | 170.2 s | 170.1 s | 169.8 s | 170.3 s | 170.0 s | 169.7 s |
| | 170.2 s | 169.6 s | 169.3 s | 169.0 s | 169.6 s | 169.6 s |
| | 21.6 q | 169.4 s | 21.3 q | 21.4 q | 169.5 s | 20.9 q |
| | 21.0 q | 169.0 s | 21.1 q | 20.9 q | 21.7 q | 20.8 q |
| | | 21.8 q | | | 21.2 q | |
| | | 21.8 q | | | 20.8 q | |
| | | 21.2 q | | | | |
| | | 20.9 q | | | | |

4.36 (1H, dd, $J = 3.6$, 1.8 Hz, H-6β), 5.60 (1H, d, $J = 3.6$ Hz, H-7α), 2.27 (1H, br s, H-9β), 4.34 (1H, br d, $J = 4.0$ Hz, H-11α), 3.00 (1H, br s, H-13α), 3.15 (1H, d, $J = 12.5$ Hz, H-14α), 5.90 (1H, br s, H-17a), 5.15 (1H, br s, H-17b), 1.00 (3H, s, Me-18), 1.06 (3H, s, Me-19), 1.67 (3H, s, Me-20), 2.27, 1.98 (each 3H, $2 \times$ OAc); $^{13}C$ NMR: Table 1.

### 3.5. Glabcensin W (**2**)

$C_{28}H_{38}O_9$, an amorphous powder, $[\alpha]_D^{22}$: −59.98° (MeOH, *c* 0.42) UV $\lambda_{max}^{MeOH}$ nm (log ε): 236.5 (3.95); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3440, 2910, 1720, 1650, 1450, 1370, 1230, 1025; EIMS *m*/*z* (rel. int.): 518 $[M]^+$ (1), 458 $[M–AcOH]^+$ (12), 416 $[M–AcOH–COCH_2]^+$ (25), 398 $[M–2 \times AcOH]^+$ (26), 356 $[M–AcOH–COCH_2]^+$ (60), 338 $[M–3 \times AcOH]^+$ (38), 323 $[M–3 \times AcOH–Me]^+$ (55), 296 $[M–3 \times AcOH–Me–H_2O]^+$ (75), 281 $[M–3 \times AcOH–Me–H_2O]^+$ (100); $^1H$ NMR δ: 4.77 (1H, br s, H-3α), 2.34 (1H, br s, H-5β), 5.07 (1H, dd, $J = 3.5$, 1.8 Hz, H-6β), 5.47 (1H, d, $J = 3.5$ Hz, H-7α), 2.24 (1H, br s, H-9β), 5.30 (1H, t, $J = 4.0$ Hz, H-11α), 2.91 (1H, br s, H-13α), 2.62 (1H, d, $J = 12.3$ Hz, H-14α), 5.93 (1H, br s, H-17a), 5.21 (1H, br s, H-17b), 0.96 (3H, s, Me-18), 1.00 (3H, s, Me-19), 1.34 (3H, s, Me-20), 2.21, 2.13, 2.03, 1.76 (each 3H, s, $4 \times$ OAc); $^{13}C$ NMR: Table 1.

### 3.6. Glabcensin X (**3**)

$C_{24}H_{32}O_7$, an amorphous powder, $[\alpha]_D^{22}$: −24.5° ($CHCl_3$, *c* 0.54). UV $\lambda_{max}^{MeOH}$ nm (log ε): 238.5 (3.32); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3500, 2910, 1725, 1635, 1365, 1230; EIMS *m*/*z* (rel. int.): 432 $[M]^+$ (48), 372 $[M–AcOH]^+$ (25), 330 $[M–AcOH–COCH_2]^+$ (100), 312 $[M–2 \times AcOH]^+$ (38); $^1H$ NMR δ: 3.82 (1H, t, $J = 3.0$ Hz, H-3α), 3.60 (1H, br s, H-5β), 5.33 (1H, s, H-7α), 2.90 (1H, br s, H-9β), 5.12 (1H, t, $J = 5.0$ Hz, H-11α), 3.13 (1H, br s, H-13α), 2.87 (1H, d, $J = 12.5$ Hz, H-14α), 5.77 (1H, br s, H-17a), 5.32 (1H, br s, H-17b), 0.89 (1H, s, Me-18), 1.18 (1H, s, Me-19), 1.28 (1H, s, Me-20), 2.15, 1.82 (each 3H, $2 \times$ OAc); $^{13}C$ NMR: Table 1.

### 3.7. Glabcensin Y (**4**)

$C_{24}H_{34}O_7$, an amorphous powder, $[\alpha]_D^{22}$: −13.0° ($CHCl_3$, *c* 0.54). UV $\lambda_{max}^{MeOH}$ nm (log ε): end absorption; IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3400, 2915, 1725, 1445, 1370, 1225, 1035; EIMS *m*/*z* (rel. int.): 434 $[M]^+$ (2), 374 $[M–AcOH]^+$ (23), 314 $[M–2 \times AcOH]^+$ (25), 296 $[M–2 \times AcOH–H_2O]^+$ (25), 281 $[M–2 \times AcOH–H_2O–Me]^+$ (100); $^1H$ NMR δ: 3.87 (1H, br s, H-3α), 3.49 (1H, br s, H-5β), 5.01 (1H, br s, H-7α), 2.82 (1H, br s, H-9β), 5.33 (1H, br s, H-11α), 2.54 (1H, br s, H-13α),

4.56 (1H, br s, H-15α), 5.38 (1H, br s, H-17a), 5.29 (1H, br s, H-17b), 1.06 (3H, s, Me-18), 1.40 (3H, s, Me-19), 1.42 (3H, s, Me-20), 2.25, 1.96 (each 3H, s, 2 × OAc); $^{13}$C NMR: Table 1.

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